The New England
Journal of Medicine

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Volume 233 OCTOBER 18, 1945 Number 16

THE REHABILITATION OF PATIENTS TOTALLY PARALYZED BELOW THE WAIST: WITH SPECIAL REFERENCE TO MAKING THEM AMBULATORY AND CAPABLE OF EARNING THEIR LIVING*

I. Anterior Rhizotomy for Spastic Paraplegia

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IF he has been properly treated, every patient with a spinal-cord or cauda equina injury who is intelligent and co-operative and has the use of the shoulder, arm and hand muscles can be made ambulatory; can have such control of the bladder and bowels as to sleep through the night without either getting up or wetting himself; can carry out ordinary activities throughout the day without soiling himself with feces or having to evacuate his bladder oftener than once every three hours; can lead a normal social life, and within the limits of his intellectual capacity, can earn a satisfactory living. Such patients can start walking without unhealed pressure sores and bedsores and, except for a small group, without the need for an inlying catheter or any substitute therefor. They have to use crutches and to wear, when ambulatory, caliper walking splints, which, however, permit them to stand or sit. These are the only restrictions to their living the same social life and having the same earning capacity that they had before becoming paralyzed.

This paper is the first of a series that describes certain therapeutic procedures that have made the attainment of these end results possible. Although my experience has been largely limited to civilian casualties of this type, there is no reason why the lessons learned there should not be applied to the war casualties of the same class.

The material analyzed in the various papers has been taken from a series of 243 patients suffering from various types of cord disease (Table 1). Most of them had had an injury to the cord or cauda equina. One hundred and thirty-five patients with cervical-cord injury are not included in this table because only 2 patients with transection lived long enough to permit adequate study. Although the most frequent symptom in the classified patients was total voluntary paralysis below the waist and the rarest one uncomplicated bladder dysfunction, the majority of patients had a combination of conditions. These patients are classified as they are in Table 1 because motor paralysis, total or partial, was the outstanding symptom in one group, just as bladder dysfunction and pain were the outstanding symptoms in the other groups.

TABLE 1. *Classification of 98 Cases of Cord Disease.*

CLASSIFICATION	LOCALIZATION			
	DORSO-LUMBAR	SACRAL	CAUDA EQUINAL	ALL CASES
Permanent functional loss:				
Total voluntary paralysis	51	4	4	59
Partial voluntary paralysis	4	6	7	17
Bladder dysfunction	0	1	2	3
Disabling pain	0	0	6	6
Transitory symptoms	7	0	6	13
Pathology:				
Injury	57	11	25	93
Epidural spinal abscess	3	0	0	3
Intraspinal tumor	2	0	0	2
Totals	62	11	25	98

The 59 cases chosen for analysis from this series were picked according to the following criteria. The patient must have lived for at least ninety days after the onset of the disease or the sustaining of the accident. He must have been rendered incapable of doing gainful labor, or its equivalent in the case of a housewife or child, by the injury or disease. Lastly, the lesion must have been at or below the second thoracic segment of the spinal cord.

Total useful voluntary motor and sensory paralysis starting at some point below the waist may be caused by a complete anatomic transection of the thoracolumbar cord below the second thoracic segment; by a partial anatomic transection of the thoracolumbar cord, which is nevertheless functionally so complete as to deprive the patient of

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Presented in part before a meeting of the Department of Veterans' Affairs at Toronto, Canada, January 18 and 19, 1945.
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all useful motor or sensory control of the bladder and rectum and all or part of the muscles of the lower abdomen, low back and legs — functional transection; by destruction of the sacral cord and adjoining cauda equina; or by destruction or compression of the cauda equina alone. This paper concerns itself only with the first group (complete anatomic transection below the second thoracic segment), and discusses a method by which the spastic paraplegia that is associated with this lesion and that cannot be splinted can be altered to a flaccid paraplegia that can be.

Anatomic Transection of the Cord Between the Second Thoracic and First Spiral Segments

Patients whose cords have been completely and anatomically transected between the second thoracic and the first sacral segment develop a so-called "mass reflex" or "maximal flexor response to a minimal sensory stimulus" below the level of cord injury as soon as they have recovered from the effects of spinal shock, provided that their nourishment is kept up and that no genitourinary-tract or other major infection or toxic state is present. The classic so-called "paraplegia in flexion" is present (Fig. 1). (There were 19 such patients in this group of 59.) There are a complete absence of all voluntary motion, a total loss of all sensory appreciation and a reversion of the bladder and rectum to a pure reflex mechanism. When the mass reflex is fully developed, the patients are so deformed that they cannot sit up in a wheel chair, much less stand erect. Under the usual methods of treatment, the bladder discharges at the slightest stimulus — such, for example, as a cold draft or a jarring of the bed, — the bowels empty at unpredictable intervals, and the patient is constantly wet or soiled, requires an inordinate amount of nursing and develops intractable pressure sores and bedsores in spite of all care. He not only cannot support himself but is a constant and severe financial drain on his friends and relatives. Such patients are social pariahs in their own sight and in that of everyone associated with them.

Despite this usual sequence of events, such transection of the thoracolumbar cord need not necessarily condemn the patient to a bedridden, filthy life. The physician and his patient should clearly appreciate that even with this severe anatomic lesion, ambulation and normal social activity can and will be the ultimate result, provided that they both have the necessary patience and give the endless attention to the details of the preliminary treatment that is so essential while the patient is necessarily bedridden and that make equally important definitive procedures possible later. This subject has been discussed elsewhere[1] and need not be dealt with again here. Suffice it to say that, by the time the patient's bone injury has healed sufficiently to permit him to stand upright without danger of collapse of the spinal column, he should have developed a reflex bladder without evidence of genitourinary-tract infection or stone formation; his bedsores, if he has had any, should be healing and his pressure sores stationary; the serum protein should be normal, the state of nutrition satisfactory, the temperature and pulse normal, and the strength of the arms and shoulders developed well beyond the pre-injury level.

Figure 1.

This patient, aged seventeen years, had an anatomic transection at the level of the fourth and fifth thoracic segments caused by concussion of the cord from a bullet wound of the body of the fourth thoracic vertebra. An active mass reflex, with adductor-flexor contractions and deformity was present, and his condition before a dorsolumbar anterior rhizotomy is illustrated.

An active mass reflex in its classic manifestation takes the form of a dorsiflexion of the great toe, a flexion of the ankle and knee, an adduction and flexion of the hip (Fig. 2) and, unless the peripheral nerves that supply them have been destroyed, contraction of the lower abdominal and spinal muscles, possibly with a spread to the adductors

and flexors of the opposite thigh. I have never seen an extension of the opposite thigh as a continuation of the original flexion response in the stimulated leg. The flexor and adductor muscles in both legs are hypertonic, and the usual flexor tendon reflexes, such as those of the hamstrings, are extremely active. The extensor tendon reflexes, such as the knee and ankle jerks, are hyperactive unless the muscle is stretched so tightly as to interfere mechanically with its contraction. The extensor

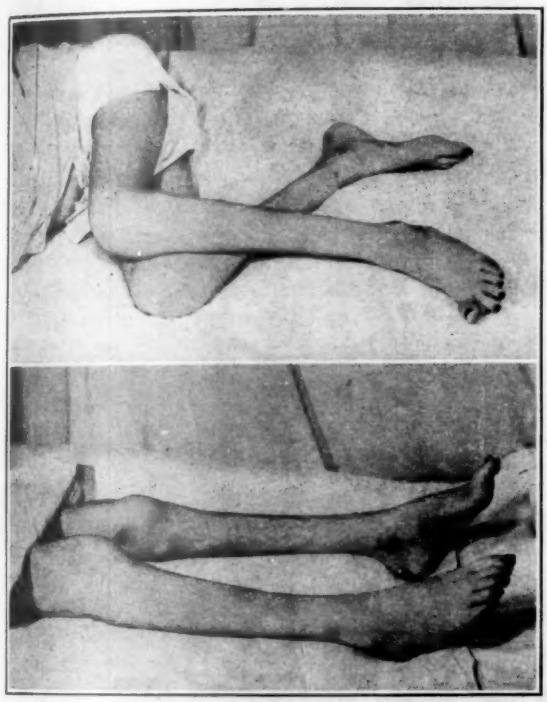

FIGURE 2.

This was a patient, aged fifteen, who had a transverse myelitis and an anatomic transection at the level of the fifth and sixth dorsal segments, caused by an epidural spinal abscess. The photographs show the mass reflex previous to dorsolumbar anterior rhizotomy and its disappearance after operation.

group of muscles themselves are not usually otherwise hypertonic. I have seen no such case with an extensor thrust.[2] Long-standing cases show extreme flexor and adductor contractures and may, unless protection is provided, develop pressure sores on the medial aspects of the knees, over the patellas and on the chest wall from constant contact between the knees themselves and between the patellas and the chest wall. Massage and manipulation and especially forcible extension and abduction of the legs lead to nothing but further increased flexion and adduction and greater contractive effort on the part of these muscles. Splinting designed to maintain the legs or feet in extension or in a position of use acts in the same way that manipulation does. If it is effective, sores develop at all pressure points and splinting has to be abandoned. Thus, unless it can be corrected the paraplegia in flexion of itself prevents ambulation.

In addition, and more importantly, the contraction of the abdominal muscles, which occurs as part of the mass reflex (except as noted above), stimulates the urinary bladder and causes it to expel its contents irrespective of amount. If an inlying catheter is in place, and whether or not tidal drainage is in use, the urine leaves the bladder around the catheter as well as through it because of the suddenness, rapidity and force of the detrusor contraction. These patients cannot be kept dry by any method and cannot be trained to control their urinary outflow so long as the mass reflex remains active. They develop pressure sores and bedsores and are constantly wet and soiled. Social life is impossible and they are soon moved out of their homes and relegated to a nursing home or public institution, where they remain until they die, usually of some intercurrent infection. Long before that happens, however, their morale has vanished and death comes as a relief.

If the mass reflex and its effects can be counteracted, splints can be applied that will permit such a patient to be ambulatory. The bladder and bowels can also be brought sufficiently under control so that the patient can be trained to go through the night without getting wet and without waking, and through the day without getting soiled and without having to empty his bladder oftener than once every three hours. This permits him to be not only ambulatory but self-supporting as well. Because I believe that the logical point of any attack designed to eliminate this abnormal reflex response is on the motor side of the reflex arc, an operation has been developed that not only changes this hypertonic spastic paraplegia to one of a flaccid type but also prevents the spreading to the abdominal muscles of any reflex motor activity in the extremities, and thus allows for control of the bladder. This is accomplished by the intraspinal division of the proper anterior spinal roots. This is preferred to division of the posterior roots because it attacks the problem, especially that of the bladder, more directly. All anterior roots are cut bilaterally from the tenth or eleventh thoracic segment through the first sacral segment. If the rhizotomy is complete, the lower abdominal and psoas muscles, the lower part of the erector spinae group and all the muscles of the lower legs become flaccid, and flexion and adduction contractures straighten out (Figs. 2 and 3). Any local tendon shortening that remains can be cared for by manipulation or a tenotomy. By the use of appropriate splints the legs can then be stabilized and hence made capable of bearing weight. With the help of crutches such patients can learn to walk and to be normally active within the limits imposed by the splints. Because the

bladder no longer empties except when it reaches its critical amount of filling or when it is deliberately stimulated, the patients also remain dry after they have learned how to urinate by the clock. For the same reason it is possible to train them so that their bowels empty themselves at the same hour once a day or once every two days. Soiling at unexpected times, with its attendant discomfort and embarrassment, is thus done away with.

This operation was first attempted in 1933 and again in 1934. Both patients had active mass reflexes and crippling adduction-flexion deformities and had been bedridden for two and a half years. Identification of the roots to be cut was attempted by counting upward from what was thought to be the fifth sacral root. This method was recognized as necessarily inaccurate — an impression that has since been verified. As a result, the relief obtained in both these cases was only partial. With the aid of tenotomies it was enough, however, to correct the flexion and adduction deformities. Both patients could be mobilized in wheel chairs, and one went home. Neither, however, could bring his bladder and rectum under sufficient control so that he could go out. Because both patients still got wet without tidal drainage, they had to use it constantly. One progressed satisfactorily at home with this limited life until his physician decided to discard the tidal drainage. He thereupon died from sepsis of the genitourinary tract. The other patient never left the hospital and also died of sepsis, which originated in a bedsore over one trochanter and led to osteomyelitis of the femur and ilium. Although the operation was far from successful, it was apparent from these cases that it was worth perfecting and probably could do what was expected of it.

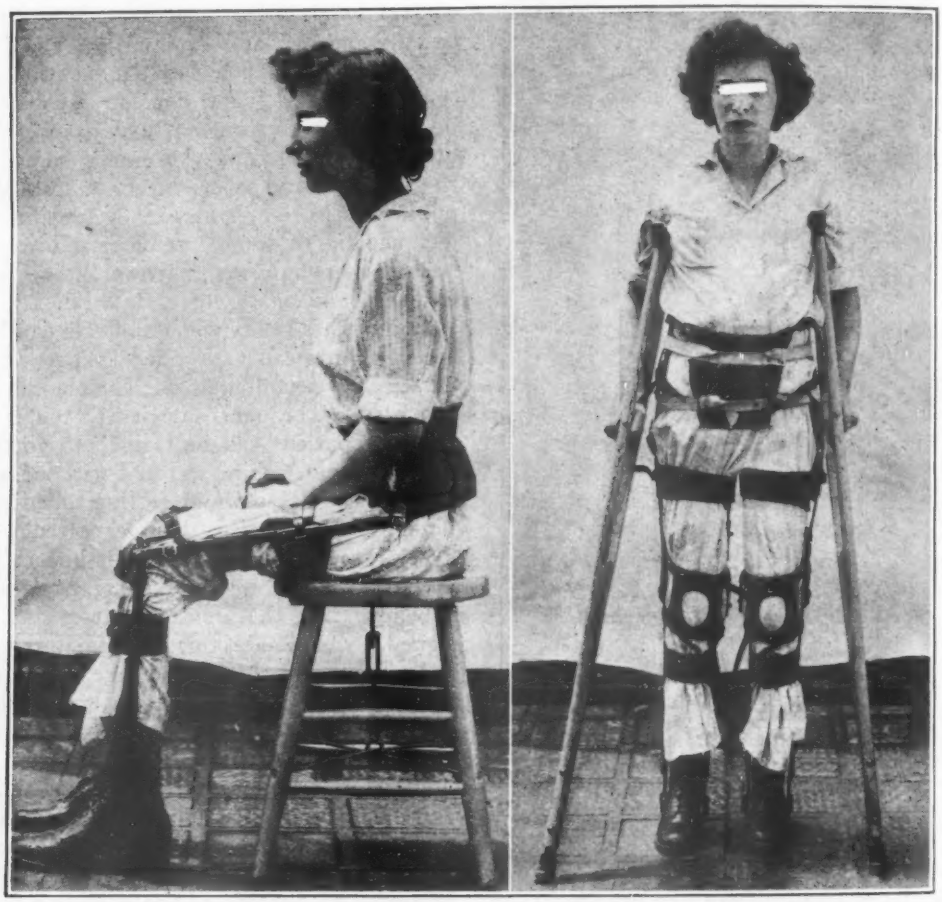

FIGURE 3.

This is the same patient shown in Figure 2. She is fully active in splints and with the aid of crutches, and has complete control of the bladder and bowel.

For this operation to be most effective a more exact method of identifying the roots was obviously necessary. It was also apparent that in addition the problems of genitourinary-tract infection and the prevention of bedsores had to be met and solved. It would be of little use to put a patient into such shape that he could become ambulatory with the aid of splints if the attainment of this end was to be denied him because of lack of control over these

two potent sources of sepsis and death. The relation of the first lumbar root to the last dentate ligament proved to be the key to the accurate identification of the roots to be sectioned, and the solution of the problems that arose out of hitherto uncontrollable infections was reached in the course of the next seven years. In the four years since 1940 sepsis of the genitourinary tract has to all intents and purposes ceased to exist in patients with spinal-cord injuries in my clinic.[3–5] It should be emphasized that in 102 patients who needed and were treated by tidal drainage, only 2 left the hospital with demonstrable evidence, including urine culture, of genitourinary-tract infection, whereas of 37 patients who needed tidal drainage but did not get it, 11 were discharged with obvious genitourinary-tract infection. Of course, tidal drainage cannot be used under combat conditions or ordinarily while the patient is being transported by air or overseas. It should be provided, however, just as soon as the wounded man has reached the hospital where definitive treatment is to be given.

The only complication that has arisen in this field is the rare formation of bladder calculi. In the past year this also appears to have been eliminated by the use of Solutions M or G as irrigating fluids.[6]

During this same period pressure sores and bedsores and the infection caused by them have also been virtually eliminated in this general group of patients.[1, 7] The incidence of bedsores developing during hospitalization dropped from 16 in 146 patients from 1930 to 1940 to 7 in 87 from 1940 to 1945. During the same periods, whereas 5 per cent of the former group were discharged with their bedsores unhealed, only 1 per cent of the latter left with the same condition. Patients admitted with bedsores already present during these two periods each made up 7 per cent of their respective groups. With these sources of trouble cared for, it was possible to resume investigation into the effects of an anterior dorsolumbar rhizotomy with a more satisfactory technic. A description of the operation as it is now performed follows.

Dorsolumbar Anterior Rhizotomy

In dorsolumbar anterior rhizotomy, the spinous process of the twelfth thoracic vertebra is identified. A bilateral laminectomy of the eleventh and twelfth thoracic vertebra is done. The dura is opened enough to see whether the conus and the start of the cauda have been exposed. If the exposure is too high, the next lowest laminas, which should be those of the first lumbar vertebra, are removed. If it is just right or too low, the laminas of the tenth thoracic vertebra, the next highest pair, are removed. After hemostasis the dura is opened for the full length of the wound. The arachnoid is then opened, and the subarachnoid space is emptied. The operator must be sure that the lumbar and sacral cord, the conus and the upper end of the cauda are exposed. The arachnoid is torn into laterally to expose the last dentate ligament (Fig. 4) on one side. If it is absent on one side it is looked for on the other. The intraspinal nerve (combined posterior and anterior roots) that encloses it (the ligament) and leaves by the dural opening next below is picked up and marked with a silver clip close to its point of exit through the dura. This is the first lumbar root. Then the next highest lateral projection of the dentate ligament is isolated. A silk stitch is

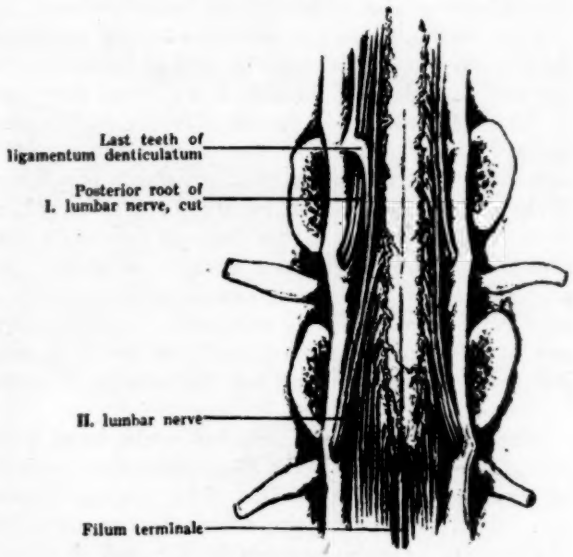

Figure 4.

The relation of the last dentate ligament to the first lumbar roots (reprinted from Frazier and Allen[10] by permission of the publisher).

put through each of these projections, and they are cut free from their dural attachments. These stitches are used as handles to rotate the cord so that the full length of the dentate ligament and the line of separation between the exit of the posterior and anterior roots from the cord can be seen.

The anterior component of the first lumbar root (identified above) is picked up, a silver clip is put on it about midway between the point where the individual filaments unite to form a single strand and its point of exit through the dura, and the root is cut lateral to the clip. The medial portion of the cut root is pulled laterally; this part can be identified by the clip on it. The traction delimits the upper fibers of origin of the next lower and the lower fibers of origin of the next higher anterior root. By following these laterally the trunks of the anterior roots of the twelfth thoracic and the second lumbar nerves can be identified and cut. By repeating this traction with each succeeding root all the other anterior roots can be identified and cut one by one. A return to the first lumbar root, which still has a clip on it, will serve for reorientation should this be necessary. If the point

of exit of any root is in question, the posterior portion of the first lumbar root, which has a clip on it next to the dura, serves as a reliable starting point for identification. All anterior roots from the eleventh thoracic through the first sacral should be cut and if possible that of the tenth thoracic also, but never under any circumstances should the roots below the first sacral be divided. All the blood vessels that can be spared should be saved. If a vessel cannot be spared it should be closed with the Bovie cutting current, no attention being paid to the resulting muscular contractions. Two blunt hooks should be available to handle the uncut nerves.

After sectioning of the desired anterior roots, all the medial portions should be pulled laterally and laid out in order and in such a way that they can be inspected from their points of origin on the cord to their points of section. The operator must make sure that no roots have been missed. The latter is easy to do, but this method of inspection makes it at once evident if a root has not been cut that should have been. I have never had to cut any posterior roots, but see no reason why this cannot be done if it is absolutely necessary. Anterior roots can be differentiated from posterior roots by squeezing them gently and noting the resultant motor activity.

After all the proper anterior roots have been cut on one side, the process as outlined above should be repeated on the other side. The operator should *not*, however, take off the silver clips or take out the dentate ligament stitches on the first side until the second is finished. They may be needed to identify roots on the second side that cannot be otherwise placed, or to rotate the cord. After the operator has satisfied himself that all the proper roots have been cut that should be, then, and only then should the clips be removed and the silk stitches pulled out. The dura should be closed tightly and the wound closed in layers without drainage.

If the patient is so deformed that the legs cannot be straightened, the laminectomy should be done in the lumbar-puncture position. If this position is used, pads must be placed under the patient's flank to make the spine level. If this is not done it may be impossible to identify the structures sufficiently accurately even to expose the laminas.

I prefer intravenous Pentothal Sodium on an avertin base as an anesthetic. Blood should be available for transfusion during operation, — since many of these patients do not stand a long operation well. The operator should not hesitate to include part of any old laminectomy scar in the new incision, but should first identify the structures in the unoperated part of the field. When previous laminectomies have been done, it is worth while to take particular pains to identify the spinous process of the twelfth thoracic vertebra before starting to operate. Errors either way in locating the center point of the incision will prolong the operation and result in unnecessary removal of a large amount of bone. After operation these patients redevelop an atonic bladder for a variable length of time. This should be cared for at once to avoid damage to the bladder wall by overdistention.

A flaccid paralysis of the legs, low back and low abdomen should be demonstrable at once after operation. It should be permanent. If spasticity redevelops, too few roots have been cut.

Operators inexperienced in neurosurgical technic should not attempt this procedure without considerable preliminary training.

Discussion

Because this operation is a permanently destructive one, the indications for performing it should never be considered lightly. For the present, at least, it should be strictly limited to those patients whose cord is anatomically transected and in whom all neural connections between the cut surfaces of the cord have been destroyed. This condition may not be easy to recognize by any means short of postmortem examination. Among other things the presence of deforming flexor and adductor spastic contractures, with the resultant impossibility of applying splints that permit weight-bearing, is not by any means conclusive evidence that such an injury exists, and does not of itself warrant a root section in the absence of more certain and fundamental evidence that the cord has actually been transected.

Among others, Head[2] has pointed out that in a true mass reflex the positive motor activity is restricted to the flexor muscles. It makes its earliest appearance as a dorsiflexion of the great toe (Babinski reflex) or as a contraction of the hamstrings, spreading later to include the other flexor muscles of the leg, the muscles of the anterior abdominal wall and occasionally the flexors of the other leg. (My experience indicates that the psoas and iliacus muscles should be added to this group.) Head holds that this is not a part of the normal postural reflexes but belongs to the ancient nociceptive mechanism, and further contends that reflex extension is evidence of incomplete transection. My experience with 51 patients with dorsolumbar cord injuries, all of whom had total voluntary motor paralysis below the level of injury, 37 of whom lived long enough to warrant attaching any significance to observations made on them and 19 of whom had a mass reflex as described above is in agreement in so far as the motor paralysis, the elicitation of the reflex and the spread of the motor response to noxious stimuli applied below the injured segment go. I have been unable to verify Head's conclusion relative to the facilitating of bladder emptying, however, in these and some 177 other patients with injuries to the cord and cauda equina of all degrees of severity and at all levels from the fourth cervical segment downward.

This subject will be discussed in more detail in a later paper. Because one of the prime purposes of performing an anterior rhizotomy is to enable the patient to regain control of the bladder, and since the difference between Head's conclusions and my observations relative to this phase of the mass reflex is one of explanation rather than one of fact, this is of less practical importance in relation to doing this operation than it appears to be.

It cannot be emphasized too strongly that the fundamental requirements prior to rhizotomy are a complete absence of voluntary motor power, a complete loss of all forms of sensory perception, a predominantly flexor or flexor-adductor contraction in the abdominal muscles and in each leg in response to a noxious stimulus applied to the sole of either foot, and the emptying of the bladder as an accompaniment of the majority of such phenomena or in response to other less noxious and more varied stimuli. On the other hand, this should not be taken to mean that the demonstration of such phenomena *necessitates* a rhizotomy to relieve the patient of his distressing or disabling symptoms. I have relieved 1 patient (not included as one of the group with an anatomic transection) with all the motor and bladder characteristics of the mass reflex by decompressing the middle thoracic cord and relieving it of the pressure exerted on it by an extradural malignant tumor. Although neither voluntary motion nor sensation returned postoperatively, so far as any observation short of postmortem examination went the cord appeared to be entirely normal. Instead of the spastic paraplegia and mass reflex that was actually present and presumably indicated an anatomic transection, the patient should have had the flaccid paraplegia of a physiologic transection before as well as after the operation.

A shrunken or hypertrophied bladder, such as is associated with prolonged suprapubic or urethral catheter drainage, may give every appearance of being a mass-reflex bladder, when in fact it is not. If the patient happens to have a total sensory and voluntary motor paralysis as well, the symptoms may be interpreted as representing a partial mass reflex. A rhizotomy under such circumstances is entirely unnecessary, and even if performed will not replace the essential stretching and retraining of the bladder that alone will effect a correction of the urinary symptoms.

The mass reflex may come on slowly and build itself up over a period of weeks. In a patient whose upper thoracic transverse myelitis and anatomic transection were caused by an epidural spinal abscess, the classic mass-reflex response did not appear until three months after the abscess had been drained and the wound had healed except for epithelialization. Clinically, the patient had presented no evidence of toxic absorption for a long time previous to this. Only one leg, however, showed the mass-reflex response at that time. Two weeks later the other leg developed mass-reflex responses, and it was not until one month later that the bladder first began to overflow in connection with these involuntary movements (Fig. 5). Following rhizotomy the spastic paraplegia became flaccid, and sufficient control was promptly established over the bladder so that it emptied only in response to a given constant amount of fill and stretch or to

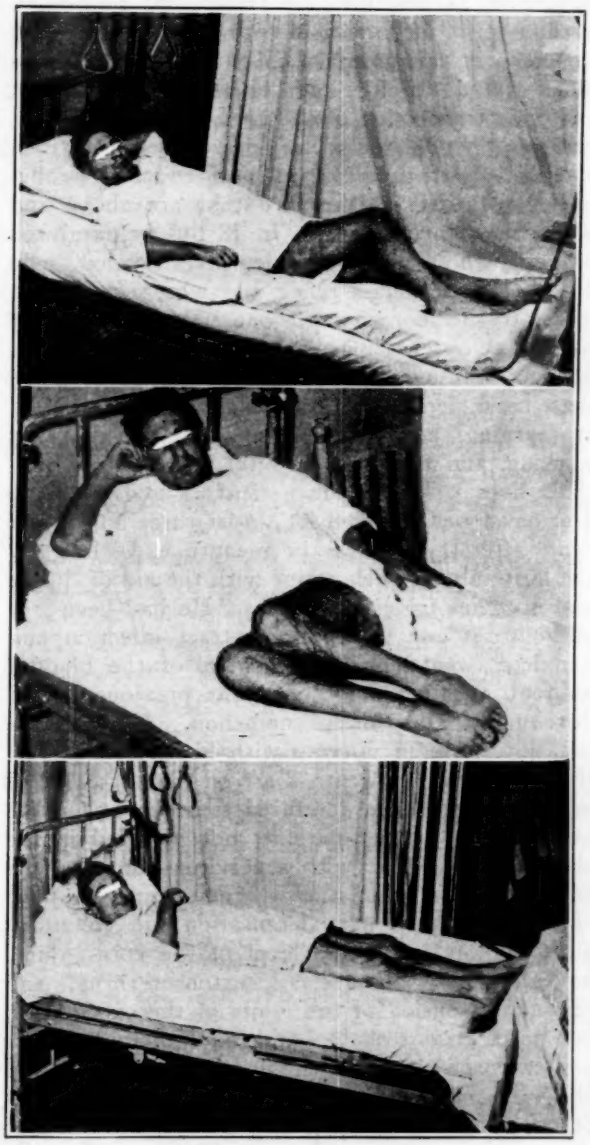

FIGURE 5.

This patient, aged thirty-six years, had a transverse myelitis and anatomic transection at the level of the eighth to tenth thoracic segments caused by an epidural spinal abscess, which was drained on July 31, 1944. A flexor response developed in the left leg on October 31, and in both legs on November 14. The bladder component of the mass reflex was added to this on December 17. A dorsolumbar anterior rhizotomy was done on December 26. The three photographs show, respectively, the unilateral flexor response, the bilateral flexor response and the condition after operation.

some such purposeful external stimulus as abdominal massage.

The absence of an extensor thrust or of a response on the part of the extensor muscles of the legs to a stimulus of the thigh, groins or abdominal wall with primary extension of all joints of the lower extremity, as described by Head[2] and considered by him to be incompatible with a mass reflex, did *not* mean in this group of 59 patients that a mass reflex would develop later or that there was an anatomic transection of the cord. Nor, in my experience, is an extensor thrust a prerequisite to a diagnosis that predicates neural connections between the parts of the cord that are above and below the damaged area. In 18 totally paralyzed patients who had a physiologic transection, who did *not* have a mass reflex and who survived an injury to the thoracic cord long enough to warrant significant observations, neither of the above phenomena was ever demonstrable. Of 12 of these that have permanent total flaccid paraplegia, 7 are earning their living, 2 are ambulant but not working, and 3 left the hospital to take up wheelchair lives. One of the patients who is working first developed an extensor thrust three and a half years after injury. In the meantime, he had left the hospital and been active with the aid of splints and crutches for eight months. He had been free of bedsores and genitourinary-tract infection and had had twenty-four-hour control of the bladder without a catheter for one year previous to the development of this phenomenon. Its presence now interferes in no way with his activities. Of the remaining 6 patients, 2 are on the ward, 3 died in the hospital, and 1 refused treatment. On the other hand, 2 other patients not included in the above group, — one with a cervical hematomyelia and the other with a midthoracic injury, — both of whom retained partial sensation and voluntary motor power below the level of the cord injury, have had not only a classic extensor thrust[2] and primary extension of the joints of the extremities, but also uncontrollable and unpredictable flexor and extensor spasms of the muscles of the legs and abdomen. I have been unable to find any previous description of this condition. This is not without its importance, because on superficial examination it could easily be confused with a true mass reflex. Another patient (included among the 10 receiving rhizotomies) who was known to have a complete absence of cord tissue for a distance of 2 cm. in the midthoracic region as the result of a shell wound showed the classic adductor-flexor mass-reflex response, as well as "primary extension of all joints of the lower extremity" on stimulation of the thighs, groins and soles of the feet. He did not, however, have an extensor thrust. All these responses were abolished after anterior rhizotomy. My experience strongly suggests, therefore, that neither the presence nor the absence of reflex activity in the extensor muscles below the level of the cord injury, even in the presence of total sensory and voluntary motor paralysis, should necessarily be considered an indication of an anatomic cord transection, and hence has no bearing on the problem of whether a given patient needs an anterior rhizotomy.

Perhaps the most important prerequisite to making such a decision, and certainly the most important one in estimating the significance of the neurologic signs that are demonstrable, is the certainty that all infections or conditions that lead to infection or toxicity in the patient are done away with. Indeed, the importance of this cannot be overstressed. Furthermore, this requirement will not necessarily or often be met by anything short of a return to normalcy of certain fundamental needs of the patient's metabolism. First, there must be no evidence of genitourinary-tract infection other than a culturable bacteriuria, and that only when an inlying catheter is in use. Pyelitis, cystitis or calculi anywhere in the genitourinary tract, as shown by clumped leukocytes, constant albuminuria, concentrated urine or other clinical evidence, may alter the characteristics of the mass reflex to any degree from complete abolition to the most minor changes and do away with the diagnostic significance of whatever neurologic changes are present. The same effect may be produced by the presence of unhealed and, more particularly, advancing bedsores and pressure sores. Spinal shock, anemia, hypoproteinemia, undernourishment, avitaminosis and the like all exert a similar effect. All these must be corrected and the patient maintained at normalcy before a decision can be reached relative to the need for an anterior rhizotomy.

Visualization of the injured area of the cord as a means of determining whether the latter is anatomically transected does not necessarily settle this question. I[8] have shown that what appeared to be intact areas in the cord exposed at operation proved later at autopsy and by clinical standards to be actually anatomic transections, whereas not a few patients with a quadriplegia that came on practically simultaneously with the accident have later walked out of the hospital and again started earning their living.[9] My experience leads me to believe, however, that no harm will follow and much good may come from a laminectomy done to relieve a spinal subarachnoid block at the site of injury — particularly if a decompression is provided early. Moreover, I believe that any patient who has both a mass reflex and a spinal subarachnoid block should have the block relieved by a decompressive laminectomy before being subjected to an anterior rhizotomy.

Results

I have performed a bilateral dorsolumbar anterior rhizotomy as described above on 10 patients. One patient was operated on three times before suf-

ficient roots were cut. In all the patients the preoperative deforming flexion-adduction spastic paraplegia has been changed to a nondeforming flaccid paraplegia. The irregular bladder emptying that kept the patient constantly wet, proved a difficult and often impossible nursing problem, led the patient to seclude himself and prevented him from carrying out any social activity, ambulation or self-support; it has been so altered that twenty-four-hour control without the use of either a urethral catheter or suprapubic drainage has been or is about to be attained in all but the first two patients. Bedsores have been healed and pressure sores have been either healed or arrested before operation in every case. No bedsores or pressure sores have developed after operation, and no complications traceable to the operative procedure have developed. Two patients have learned so to control their bowels that defecation occurs only once a day at a predetermined hour. Three others are well on the way toward attaining this end. The remainder have not done so either because — as in 4 cases — insufficient time has elapsed or because — as in 1 case — the patient did not have sufficient mental equipment to learn to do so. All but the first two either can be or have been equipped with caliper splints preparatory to ambulation and are either walking or learning to do so. The indications for the operation given above were strictly adhered to. All but one patient had an exploratory or therapeutic laminectomy over the site of the cord injury preliminary to the rhizotomy.

There were 2 other patients with anatomic cord transections and spastic paraplegia that were not considered suitable for rhizotomy. In one case the spinal nerves that innervated the abdominal muscles had been destroyed bilaterally as part of the injury that transected the cord. Because of this deficit this patient has been able to establish a workable although incomplete bladder control. After eight years of genitourinary-tract infection and resultant inhibition of the mass reflex, proper and persistent training has finally made splinting and ambulation also possible, despite the presence of a demonstrable but not particularly active characteristic mass reflex. Constant intelligent care has also prevented the development of deformities and pressure sores. Control of the bowels is maintained with the help of enemas. Under the circumstances, rhizotomy could add little or nothing to this patient's mobility and was considered inadvisable. The other patient presented all the indications for rhizotomy, but because she was a moron and incapable of such co-operation as would have been necessary to teach her to control her bladder and learn to walk, her family was advised not to have a rhizotomy performed.

A third patient who had a transected cord but did not have a rhizotomy was able to lead a wheelchair life in spite of a spastic paraplegia and moderate but not disabling flexion-adduction deformities of the legs. Bladder control was absent. The mass reflex was characteristic and active, and rhizotomy was advised, but the patient refused it. Another similar patient preferred life in a public institution to rhizotomy and also refused operation.

Five early cases were not operated on because of inability to control sepsis and hypoproteinemia before they died.

Summary

Bilateral intraspinal division of the anterior roots of the eleventh thoracic through the first sacral spinal nerves is recommended as a means of changing a spastic to a flaccid paraplegia in patients with an anatomic transection of the spinal cord at any point between the second thoracic and the second sacral segments preliminary to making the patients ambulant and to providing them with complete twenty-four-hour control of micturition so that they may again become active members of their community and be self-supporting.

The need for establishing certain stringent preoperative indications is emphasized. These requirements are described, and certain confusing aspects of them are discussed.

The technic of the operation is described.

The application and results of the operation in 10 of 19 patients with spastic paraplegia following anatomic transection of the spinal cord are reported.

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COBRA VENOM IN THE TREATMENT OF ANGINA PECTORIS*

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BOSTON

THE usefulness of cobra venom for the control of pain was first suggested in 1929 by Monaelesser.[1] In 1936, Bullrich[2] reported favorable results in the treatment of angina pectoris. Seven patients — 5 with syphilitic aortitis and 2 with coronary arteriosclerosis — received 1.25 to 5.0 mouse units§ of cobra venom intravenously; the succeeding doses and frequency of administration varied in each case. The physiologic and pharmacodynamic effects of cobra venom have been investigated by Macht,[3, 4] who demonstrated that its effects were those of a sedative acting on the thalamus. He[5] reported relief of various types of pain in approximately 70 per cent of 200 patients, including 2 with angina pectoris. The method and duration of administration in these 2 cases were not described. In 1940, Parsonnet and Bernstein[6] used cobra venom successfully in 5 patients with stenocardia at rest unrelieved by any medication except morphine sulfate. The medication was given intramuscularly in doses of 5 to 10 mouse units daily for three to five days, then 10 units every other day for five or six doses and finally 5 units once or twice weekly. In 3 cases complete disappearance of pain occurred after two, three and five days, respectively. In 4 patients no further attacks at rest were experienced, although 2 of these had pain on exertion; in the remaining case pain returned on two subsequent occasions but was relieved each time by an additional course of treatment.

The literature thus records 14 cases of angina pectoris treated by the injection of cobra venom with uniformly good results. It must be pointed out that all three investigators evaluated the benefits of therapy by the clinical history alone. The clinical evaluation of therapy in angina pectoris is, however, difficult because of the natural variation in the course of the disease and because psychologic factors cannot be adequately controlled. It has been repeatedly demonstrated that when judged by the clinical history, beneficial results can be obtained with the use of placebos as frequently as with other medication,[7–9] so that objective studies are necessary. The present study was undertaken as part of an objective evaluation of methods of treatment in this condition, which has up to the present included approximately seventy different therapeutic measures.[10]

Material and Methods

Twelve patients — 10 men and 2 women — with angina pectoris of coronary arteriosclerotic origin had been studied for various periods of time — 9 cases for two to seven years and 3 cases for two to four months in a special clinic devoted to angina pectoris. During the period of observation the frequency of the attacks in daily life became well known. The amount of work that could be performed under standardized conditions before pain developed had been determined on many occasions according to the method previously presented.[11] The patients' responses to many different methods of therapy were established. Four responded strikingly to many different forms of treatment. Following the sublingual administration of 0.3 mg. of nitroglycerin they were able to do 100 per cent more work than was possible without medication, and according to the scheme previously described[10] they were classified as Group 1 patients (marked reactors). Three of the patients responded in a moderate degree to therapy in that they were able to do approximately 50 per cent more work after nitroglycerin, and were termed Group 2 patients (moderate reactors). The remaining 5 patients failed to respond to any of the usual methods of treatment, including nitroglycerin, and were termed Group 3 patients (nonreactors).

The initial periods of therapy with other drugs served as a basis for comparison. Cobra venom¶ in doses of 10 to 20 mouse units (1 to 2 cc.) was injected into the deltoid muscle at least daily for periods ranging from three to seven days or until a therapeutic response was obtained. Clinical evaluation of the response and standardized exercise-tolerance studies were made at daily to weekly intervals throughout the period of study. Local pain, during and continuing for a short time after each injection, occurred almost uniformly. This prevented perfect control, since saline solution, which was used as a control injection, is not painful.

Results

Effect on Exercise Tolerance and Pain

The intramuscular administration of cobra venom resulted in a 25 to 75 per cent increase in the standardized exercise tolerance in 7 of the 12 patients studied (Table 1); they included 3 of the 4 patients in Group 1, 1 of the 3 patients in Group 2 and 3 of the 5 patients in Group 3. In 6 of the 7 patients in

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§A mouse unit is the minimum lethal dose for a 20-gm. mouse.

¶The cobra venom used in this study was supplied by Hynson, Westcott and Dunning Company, Baltimore, Maryland.

Groups 1 and 2, nitroglycerin was considerably more effective (Table 1). On the other hand,

TABLE 1. *Comparative Effect of Nitroglycerin and Cobra Venom on the Standardized Tolerance of Patients with Angina Pectoris.*

Case No.	No Medication	Two Minutes after Sublingual Administration of Nitroglycerin	After Three or More Injections of Cobra Venom
Group 1:			
1	24	36	44
2	35	75	48
3	40	108	42
4	20	44	33
Group 2:			
5	20	32	41
6	45	62	51
7	36	44	30
Group 3:			
8	4	4	13
9	10	10	20
10	11		20
11	20	20	28
12	40	41	33

in 3 of the 5 patients comprising Group 3 the injection of cobra venom resulted in a significant increase in ability to do work. In 2 of these patients cobra venom is the only drug out of fifty-seven tested to date that has enabled them to do more work or has resulted in demonstrable clinical improvement. The increase in ability to do work under standardized conditions was paralleled by a decrease in the frequency of attacks in daily life.

The effect of cobra venom is best illustrated by the results in Case 5 (Fig. 1). This patient, a 69-year-old widow, had had angina pectoris for seven years and had been observed in the Angina Clinic for five years. Attacks usually occurred one to three times daily. The usual amount of exercise under the standardized conditions necessary to induce angina was twenty to twenty-five trips. Following the administration of nitroglycerin the patient was able to do thirty-two trips. Treatment with cobra venom was begun with a single dose of 10 mouse units. The exercise tolerance and the clinical course remained unchanged during the next fourteen days. Thereafter daily injections of 10 mouse units each were given. On the fifth day a marked rise in exercise tolerance occurred, and the patient experienced no pain during her daily routine. After seven injections of cobra venom, daily injections of saline solution were substituted. During the next eleven days there were no attacks in daily life. Because the standardized exercise tolerance seemed to be decreasing, a second course of seven daily injections of cobra venom (10 mouse units) was given. Again improvement was observed, beginning on the fifth day. Six days after discontinuing medication, a decrease in exercise tolerance was observed. By the ninth day the exercise tolerance had returned to the control levels and attacks in daily life returned.

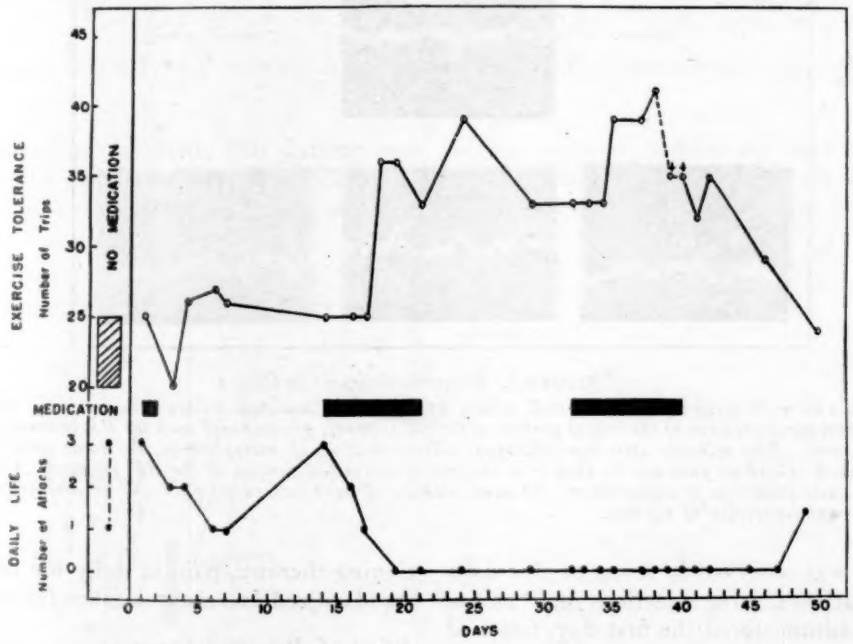

FIGURE 1. *The Effect of Cobra Venom on the Exercise Tolerance and the Number of Attacks of Pain in Daily Life in Case 5.*

Effect on Electrocardiogram after Exercise

Electrocardiographic studies[12, 13] were carried out in 2 of the 7 patients who benefited by the injection of cobra venom, and the results were compared with those observed following the administration of nitroglycerin. In contrast to the effect of nitroglycerin, cobra venom did not prevent the electrocardiographic changes induced by exercise. Despite the

absence of pain, the electrocardiogram following exercise was identical with that observed when the patient was receiving no medication and experienced pain on exertion (Fig. 2).

Time of Onset of Effect

In 5 patients, seven injections of 10 mouse units each were given intramuscularly over a period of nine days — daily except Saturday and Sunday. The increase in exercise tolerance and decrease in daily attacks began about the fifth day, and the maximum effect was observed in seven to nine days (Fig. 3). In 6 patients, three injections of 10 mouse units each were administered the first day, followed by daily injections as noted above. In these cases the effect first became evident in three days, with a maximum effect on the fourth and fifth days. The results in 2 of these patients are illustrated in Figure 4. In 1 patient given 2 cc. three times the first day severe toxic symptoms ensued and further therapy was impossible (see below).

Maintenance of Effect

In 5 cases injections of cobra venom were discontinued after a maximum effect was reached. Approximately six days later the pain returned during daily life and there was a measurable decrease in the standardized exercise tolerance (Fig. 3). In 2 patients 10 units (1 cc.) was injected semiweekly (Fig. 4) and continued for four and a half to seven weeks. One patient (Case 5) treated for four and a half weeks remained free from pain in daily life for three weeks and the increase in standardized exercise tolerance persisted. Because of the return of pain the dose was increased to 15 and then 20 mouse units (given twice), but further treatment had to be discontinued because of severe chest pain accompanied by nausea, vomiting and diarrhea. The other patient (Case 11), treated for seven and a half weeks, continued to be relatively free from pain in daily life for six weeks. In spite of continuing therapy, pain in daily life returned and the standardized exercise tolerance fell to control levels.

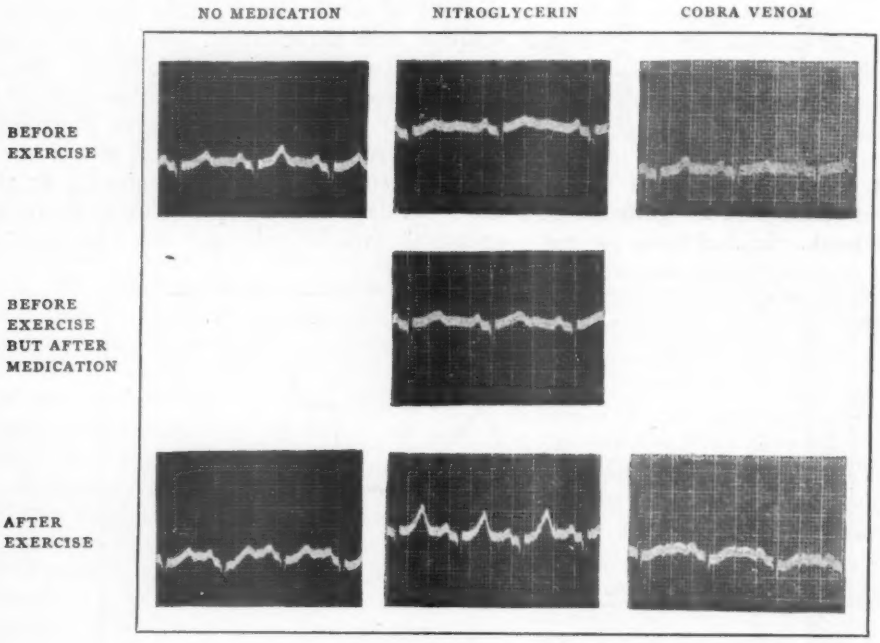

FIGURE 2. *Electrocardiograms in Case 4.*

When no medication was administered, twenty trips over the two-step staircase caused pain and an average depression of the initial portion of the ST segment, as compared with the PR interval, of 1.3 mm. Two minutes after the sublingual administration of nitroglycerin, the same amount of work caused no pain and no change in the level of the initial portion of the ST segment. After six daily injections of cobra venom, the same amount of work caused no pain and an average ST segment depression of 1.4 mm.

Effect of Repeated Courses

In 5 cases, one and a half to eight weeks after the effect of the first course of therapy had disappeared, a second and in 4 of them a third course of therapy (7 injections in nine days) was given (Table 2, Figs. 1 and 4). In 4 of these cases essentially the same results were obtained by the second

TABLE 2. *Effect of Repeated Courses of Therapy with Cobra Venom on the Standardized Exercise Tolerance.*

Case No.	No Medication	After Injection of Cobra Venom		
		first course	second course	third course
1	26	40	40	
4	18	34	32	34
5	25	36	38	34
8	4	13	11	8
10	11	20	13	10

course of therapy as followed the first. One patient (Case 10) was benefited by the first course but did not respond to the second or third course. The

Toxic Effects

Local pain occurred in every case, even when the drug had resulted in disappearance of the pain of

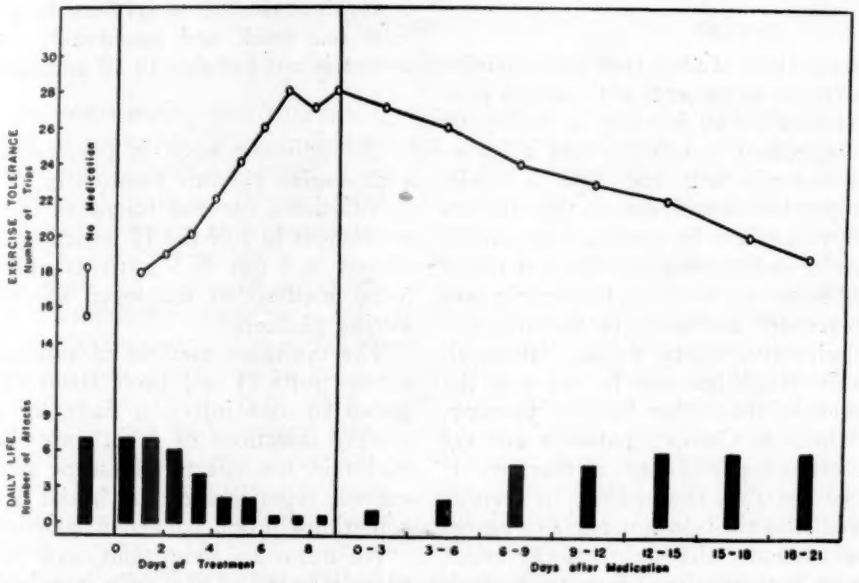

FIGURE 3. *The Effect of Seven Injections of Cobra Venom in Nine Days (average of observations in 5 patients).*

reasons for this are not evident; this patient was unresponsive to the usual medication employed in angina pectoris. In 2 patients a therapeutic response

angina pectoris, but in no case was this severe enough to warrant discontinuation of therapy. When 10 units was injected daily, no toxic effects were

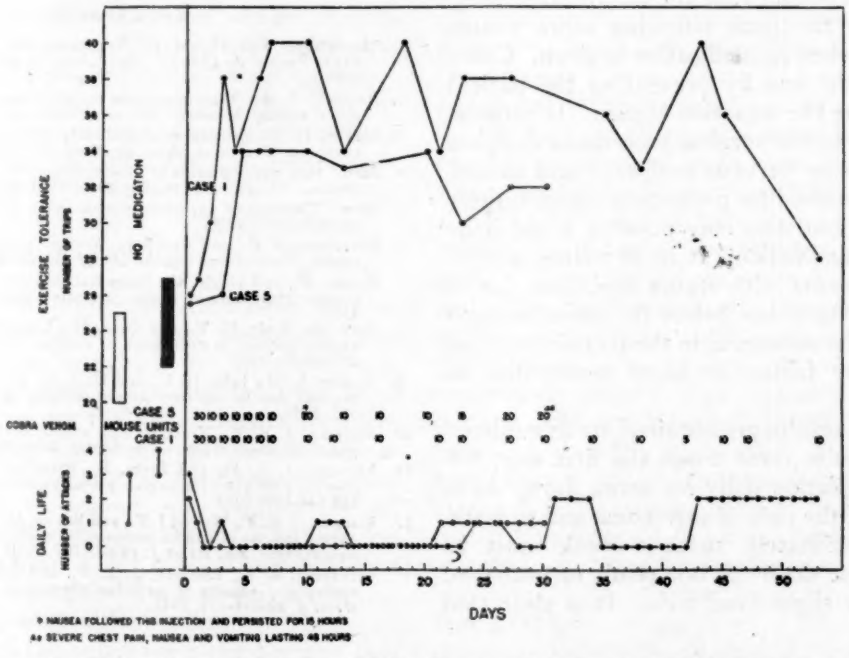

FIGURE 4. *Time of Onset of the Effect of Cobra Venom and the Result of Continued Therapy in Cases 1 and 5.*

was obtained with each course of therapy. In 1 patient (Case 8) the third course of therapy was less effective than the first or second.

observed in any patient. One patient, who received 20 mouse units three times in twenty-four hours, noted severe chest pain, nausea, vomiting and

diarrhea, which disabled her and prevented further therapy. As noted above, similar symptoms occurred in a patient in whom the dose was increased from 10 to 20 mouse units (Fig. 4).

Comment

It is evident from these studies that the administration of cobra venom to patients with angina pectoris is often followed by an increase in ability to work under standardized conditions and a corresponding improvement in daily life. This occurs in a fairly large proportion of patients, so that the results with cobra venom are in general comparable to those observed by us following any effective medication. It should be noted, however, that in the case of patients who respond markedly to the administration of nitroglycerin, cobra venom, although effective, is usually much less so. In one way the drug is more beneficial than other forms of therapy, for it may be helpful to Group 3 patients who are unresponsive to other types of medical therapy. It should be pointed out that the increase in exercise tolerance observed after the injection of cobra venom in some of these patients, although actually small, represents a large increase in ability to perform work.

There are, however, definite drawbacks to the use of the drug. Most important is the fact that it fails to have any effect on the underlying processes responsible for the discrepancy between the demands of the myocardium and the supply of blood. This is evidenced by the fact that the electrocardiogram after exercise is the same following cobra venom therapy as it is when no medication is given. Cobra venom apparently acts by preventing the patient from experiencing the sensation of pain. It is therefore comparable to the surgical procedures designed to interrupt sensory nervous pathways and should, we believe, be reserved for patients in whom surgery is contemplated but who may possibly avoid it by the use of this medication. It is, of course, worthy of a trial in patients with status anginosus due to any cause, but the delay before its effect becomes apparent limits its usefulness in the treatment of the pain of coronary failure or acute myocardial infarction.

The optimum results are obtained by administering 10 mouse units three times the first day, followed by one injection daily for seven days. As in the treatment of the pain of carcinoma and so forth, injections approximately twice a week must be continued. These doses do not result in untoward effect except for slight local pain. It is clear that even with this regime escape from the effect of cobra venom occurs.

Another, although less important, drawback to the use of this drug is the cost of therapy. Furthermore, since the injections must be given daily for at least one week and semiweekly thereafter, cobra venom is not suitable to all ambulatory patients.

Summary

The administration of cobra venom to patients with angina pectoris resulted in an increase in the standardized exercise tolerance and in clinical improvement in 7 of the 12 patients studied. This occurred in 4 out of 5 patients unresponsive to the usual medication employed in the treatment of angina pectoris.

The optimum method of administration was 10 mouse units (1 cc.) three times the first day, followed by one injection daily for seven days; biweekly injections of 1 cc. were then necessary to maintain the effect. If escape from the drug occurred, repetition of the initial course of therapy sometimes produced beneficial effects.

No untoward symptoms occurred with the dose recommended. Local pain invariably occurred, but in no case was it severe enough to warrant discontinuance of treatment.

Cobra venom does not prevent the electrocardiographic changes associated with exertion in patients with angina pectoris. Its action is therefore not that of coronary vasodilatation.

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MEDICAL PROGRESS

TUBERCULOSIS

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IN spite of four years of war and deprivation there has been, as yet, no indication of an anticipated and dreaded increase in tuberculosis mortality rates. On the contrary, the death rate has shown a gratifying decline. But, as Moriyama and Yerushalmy[1] point out, the danger has not yet passed.

Tuberculosis is a chronic disease and the current death rate is not a sufficiently sensitive index of changing conditions as they occur. The population may still be benefiting from the favorable rates of previous years; adverse conditions may have an accumulative effect that will be felt only in the future. In continental United States there was a decline of 1.2 per cent in the mortality rate of 1943 as compared with that of 1942. In Massachusetts, for the same period, however, the rate increased from 37.5 to 42.7 per 100,000 population, but the significance of this rise is not clear. The provisional 1944 death rate for the entire United States was 40.8, a decrease of 4.2 per cent from the rate for 1943.[2]

In Europe the situation regarding tuberculosis is extremely serious.[3] A general increase in tuberculosis mortality has been noted since 1942. Great Britain, the Scandinavian countries and Switzerland have withstood the years of trial remarkably well, but in France, Belgium, the Netherlands, Germany, Austria, Czechoslovakia, Hungary, the Balkans, Italy and Poland the number of cases is increasing. Conditions are especially grave in the Netherlands, the Balkans, Italy and Poland.

MASS X-RAY SURVEYS

The photofluorogram or miniature x-ray film has become established as the most frequently used screening device for searching out tuberculosis in large groups of people. It is credited with being the principal factor for the low incidence of tuberculosis in the Army (judging from the annual hospital admission rate),[4] and its application to case-finding is certain to become even more universal. In fact, Surgeon-General Thomas Parran[5] has listed x-ray examination for the entire population first among the essentials of an effective tuberculosis-control program for the Nation.

On the basis of the extensive x-ray surveys that have been carried out the past few years by military and civil agencies, certain general statistical conclusions can now be reached. In New York City, for example, it is estimated that between 1933 and 1943 approximately 2,500,000 persons had chest x-ray films taken for the purpose of discovering previously undetected disease and that about 2 per cent of these had evidence of chronic pulmonary tuberculosis.[6] Approximately one third of these persons (0.6 per cent) were classified as having lesions of clinical significance, but further investigation usually demonstrates that about half of them (0.3 per cent) can eventually be considered arrested.

The statistics from other areas are quite comparable. In Canada, it has been found that the distribution of the disease is fairly uniform throughout the country, and that only 40 per cent of those who are diagnosed as having pulmonary tuberculosis are referred to sanatoriums for further study and treatment.[7] In England, too, where miniature mass radiography has been used to detect unsuspected thoracic abnormalities, the London County Council reports the examination in one year of 45,682 persons, 112 of whom (0.2 per cent) were advised to accept hospital or sanatorium treatment.[8]

It has been estimated that within the past four years approximately 18,000,000 selectees and 3,000,000 industrial workers will have had chest roentgenograms for tuberculosis. The magnitude of the task — and the accomplishment — is just beginning to be realized as statistical data appear in the journals. From North Carolina, for example, Zanca and Herpel[9] report a rejection rate of about 0.5 per cent for all types of tuberculosis in 100,000 consecutive selectees given chest photofluorograms. From Michigan, Kinzer[10] analyzes the results on 105,141 selectees and finds that pulmonary tuberculosis was the cause for rejection in 999 (0.95 per cent). These figures are lower than the average, and they reflect creditably on the tuberculosis-control programs in those areas and on the local draft boards that weeded out manifest cases of tuberculosis before they reached the induction centers. For comparison it is well to cite the statistics of Gould,[11] who found that, in the chest x-ray films of 685,817 persons taken by the United States Public Health Service, reinfection tuberculosis was detected in 1.4 per cent. This figure is regarded as being representative of the general incidence of the disease as determined by mass fluorography.

Certain industries, all general hospitals and some institutions are especially fertile fields for x-ray surveys. "Industrialization," says Hilleboe,[12] "appears to be assuming a prominent role as a causal factor of high tuberculosis mortality rates." Of the more than a million workers examined by eight field units of the United States Public Health Service

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from 1942 to 1944, about 1.5 per cent had x-ray evidence of reinfection-type tuberculosis. It is planned, soon, to send twenty such x-ray units to local communities, at the request of state health departments, and to assist states and cities in starting mass x-ray surveys among industrial workers and among the 15,000,000 persons admitted each year to general hospitals.[13]

General hospitals are still not utilizing routine chest roentgenography to the extent that seems advisable, and this point is stressed in a number of recent articles. Small film roentgenography, as a matter of fact, is admirably suited to case-finding in general hospitals, since there is no expense entailed in assembling people for the study and the films may be interpreted by staff roentgenologists. Besides, in general hospitals, facilities already exist for completing clinical examinations and providing ambulatory care.[12, 14]

"Miniature chest radiography," say Scatchard and Duszynski,[15] "can no longer be called experimental." Then they add significantly: "It is now possible to x-ray every admission to all general hospitals as part of the routine. The small film of the chest provides an excellent case-finding method, as well as an extremely valuable diagnostic procedure." Of 3000 consecutive x-ray examinations made by these investigators, significant thoracic lesions were noted in 1070 (35.7 per cent). Of 1832 patients admitted to the hospital, 36 unsuspected cases of tuberculosis were discovered. Wilson[16] has also commented on the indispensability of the x-ray for the early diagnosis of chest lesions — before they reach a hopeless, advanced stage. Mattison,[17] too, believes that case finding among symptomatic persons or contacts is either entirely inadequate or too limited in scope to discover an appreciable number of patients in the minimal stage of tuberculosis. Mass roentgenography, he suggests, provides a method for reducing the time interval between the onset of the disease and the discovery of its presence.

If additional evidence were needed to prove this point, the work of Bloch and Tucker[18] at the clinics of the University of Chicago could be cited. Their study of 15,000 patients whose chests were fluoroscoped regardless of their complaints revealed a tuberculosis incidence of 1.4 per cent, and on this basis, it is estimated that 600,000 persons with active tuberculosis will come under medical care this year — without the underlying disease being suspected.

In addition to the general hospitals, case-finding is also profitable among the inmates and employees of institutions for the care of those with chronic diseases. Tuberculosis sanatoriums themselves are not entirely blameless as a source of new cases, and they may, in a way, be a reservoir rather than a trap for the disease. Myers[19] acknowledges the need of a place for the isolation of every contagious case of tuberculosis, but he goes on to say: "Our sanatoriums have removed from homes and communities many contagious cases, but they have created a serious problem by spreading tubercle bacilli from patient to patient, to personnel and to visitors. Only recently has any worth-while attention been paid to the protection of others against the tubercle bacilli of institutionalized patients."

There can be no question that the personnel of some tuberculosis sanatoriums are often inadequately protected against the disease. Tuberculin-testing and frequently repeated x-ray examinations of sanatorium staff members are essential for the prompt discovery of infected persons. In this respect the program of employee care furnished by the Cheshire Joint Sanatorium in England is commendable.[20] There, each new member of the personnel is given a physical examination, a tuberculin test and a chest x-ray examination, and in addition, the erythrocytic sedimentation rate is determined. Those with positive Mantoux reactions are re-examined semiannually. Those with negative ones are re-tested at monthly intervals, and special care is taken to provide them with proper guidance and treatment if the Mantoux test becomes positive.

In mental hospitals, where the incidence of pulmonary tuberculosis is high and where there has been a grave, wartime reduction in personnel, the problem of tuberculosis control is especially serious. In Oklahoma, for example, the incidence of tuberculosis in the mental hospitals is ten times greater than among the general population.[21] As a matter of fact, 7 per cent of all the state's tuberculosis deaths in 1943 were traceable to mental hospitals. In New York State, the average annual tuberculosis death rate in 1939–1941 was 593.6 per 100,000 for the mentally ill, whereas it was only 46.8 for the state as a whole.[22] The patient population in the mental institutions of the state was only 0.6 per cent of the total population, but it accounted for 8.1 per cent of all tuberculosis deaths.

It is no wonder then that employees in mental hospitals show a greater incidence of tuberculosis than those employed in other occupations. Among the 14,228 employees in twenty New York mental institutions, 156 (1.1 per cent) showed x-ray evidence of clinically significant tuberculosis, an incidence that is almost twice as great as that of workers in general industrial occupations. Surprisingly, x-ray examination of 5735 applicants for institutional employment revealed also that 61 (1.1 per cent) had significant pulmonary tuberculosis. This high figure, which is twice that of the general population, is a reflection of the low economic level of the applicants for work in mental hospitals.

The So-Called "Early" Lesion

Thanks to mass x-ray surveys, the majority of tuberculosis cases that are being discovered are in the minimal stage. Since the term "minimal"

refers only to the extent of the lesion as visualized on the x-ray film, and not to its degree of activity, the designation incompletely characterizes the lesion. From the standpoint of therapy and prognosis it is far more important to know whether the suspected area is active, inactive, arrested or healed. But it is precisely this point — the evaluation of the potential risk of progression — that is most difficult to determine in advance. A few criteria are, nevertheless, being gradually established.

In the first place, some impression of the stability or instability of a lesion can be gained from its appearance on the x-ray film. According to Reisner and Downes,[23] the exudative lesion usually has ill-defined borders and is "soft" in appearance, the productive and fibrotic lesion is composed of discrete nodular densities or strand-like linear densities, the exudative-productive lesion is a combination of these two, and the fibrocalcific lesion usually consists of multiple, scattered, small, sharply defined, nodular densities. If the lesions are differentiated in this way, it is found that the risk of progression is far greater in the exudative or the exudative-productive group than it is in the other two. The risk is greatest in the first year, but it extends beyond five years. The age of the patient or the presence of tubercle bacilli in the sputum at the time the lesion is discovered is less significant than the character of the lesion. The authors conclude: "It is necessary to regard all those exhibiting minimal lesions of a predominantly exudative character as of potential seriousness. It must also be emphasized that the intensive supervision of the case over extended periods of time is of the utmost importance."

Amberson[24] agrees that as much information as possible should be sought from the x-ray film, and even though one cannot pretend to interpret shadows in terms of exact pathology, the aim, at least, should be in that direction. He emphasizes, of course, that good visualization of a suspected lesion must be obtained before any attempt at interpretation can be made. In this connection, it is worth while to remember that the anteroposterior lordotic projection may be a distinct aid in bringing out lesions that are hidden behind a clavicle in the routine, posteroanterior roentgenogram. The technic of obtaining this type of film is described in two brief and easily readable articles.[25, 26]

The concept of prephthisical tuberculosis has been advanced by Mayer and Rappaport[27–30] to clarify the diagnosis and treatment of early lesions. The term "prephthisical tuberculosis," according to the authors, is applied to all tuberculous lesions in the chest that precede the development of chronic pulmonary tuberculosis or phthisis. In addition to those with persistent but stable x-ray lesions, prephthisical tuberculosis includes those who have recently acquired tuberculin sensitiveness and those who have had a recent episode of simple pleurisy with effusion. Mayer and Rappaport contend that it requires observation to determine whether a given lesion is in a phthisical or prephthisical stage. Every tuberculous lesion must be assumed phthisical until proved otherwise. But, to treat all tuberculous lesions as if they were phthisical is wrong because the majority of them show spontaneous arrest and healing. It is argued, furthermore, that young persons with recently acquired prephthisical lesions should not be exposed to contact with open phthisis in tuberculous wards until observation has proved the diagnosis and laboratory tests have demonstrated the contagiousness of their disease. They conclude: "Immediate treatment is most important in phthisical lesions. Prolonged observation with frequent x-raying is most important in prephthisical lesions."

Amberson's[24] viewpoint is not wholly in agreement with this. He admits the difficulty in distinguishing lesions that threaten to advance and must be treated from those that spontaneously become arrested without any enforced alteration in the patient's mode of life. But it is not enough to glance at an x-ray film and decide what adjustments the patient should make. All identifiable factors must be considered in the evaluation of a given case. Amberson recommends that patients with minimal lesions be hospitalized for about ten days to allow for an intensive work-up of their cases. Since the rate of evolution of unstable lesions, particularly in young people, is extremely variable, observation in a hospital is a definite necessity until the trend is determined and effective treatment is established. To take the point of view that these patients need nothing more than periodic x-ray examination, that most of these infiltrates will heal without treatment and that treatment is not necessary until they have undergone necrotic changes is unwarranted. The time to start effective treatment, according to Amberson, is before the phase of advanced tuberculosis has asserted itself. Treatment should be individualized, but for the young person, prescribed bed rest usually varies from three months to a year. Thereafter graduated exercise is begun, and regulation of the patient's daily life should continue for the next year or two.

The presence or absence of tubercle bacilli in the patient's sputum or gastric contents may be an uncertain guide in the evaluation of his clinical status. If the sputum is negative by culture or guinea-pig inoculation, — negative stained smears are worthless in such cases, — gastric specimens should always be obtained whenever there is a suspicious roentgenologic lesion. Feld[31] has shown that the person with a negative sputum culture but with a positive gastric test is not entirely innocuous. Some of these patients eventually develop positive sputums. He recommends treating a patient with a positive gastric content exactly like a positive sputum case. At the Muirdale

Sanatorium it is current practice to keep such suspicious cases for eight weeks, during which time intensive laboratory studies are carried out. At the end of this period, a patient may be discharged, if examination warrants it, with the diagnosis "no clinical evidence of active tuberculosis."

Medlar and Reid,[32] on the other hand, believe that patients can be classed as "pathologically active, clinically inactive" when the lesion shows no evidence of progression and yet tubercle bacilli can be detected in the sputum by culture or guinea-pig inoculation. These investigators performed sputum and gastric examinations on 252 employes in the Home Office of the Metropolitan Life Insurance Company. They found tubercle bacilli in 66 persons, 63 of whom either had clinically active tuberculosis at the time of the examination or had had sanatorium treatment for active tuberculosis in the past. Judging from their statistics, those with a minimal disease have as difficult a time in eradicating tubercle bacilli as do those with moderately advanced disease. They conclude, "The demonstration of tubercle bacilli in ex-sanatorium patients at work simply stresses the chronicity of a tuberculous infection regardless of the extent of the disease."

Chemotherapy and Antibiotics

No chemical agent has yet been discovered that is effective, safe and acceptable for general use in the treatment of clinical tuberculosis. Great interest — from an experimental standpoint — continues to center on the sulfones, especially promin (sodium *p,p'*-diaminodiphenylsulfone-N,N'-didextrose sulfonate) and diasone (disodium formaldehyde sulfoxylate, 4,4'-diamino diphenylsulfone).

Research during the past five years has demonstrated that promin has a marked deterrent action on tuberculosis in guinea pigs, that it can bring about resolution of some experimental tuberculous lesions already established and that it can lengthen the survival time of infected animals. Logically, therefore, it could be assumed that, by the inoculation of guinea pigs with virulent tubercle bacilli, and by allowing the bacilli to disseminate and multiply before initiating chemotherapy with promin, it might be possible to stimulate the natural immunogenic processes of the animals. Such an experiment could be regarded as being analogous to vaccination with whole bacilli — with this difference, that chemical attenuation of the micro-organisms might be accomplished in vivo after inoculation.

This hypothesis has been tested recently by Feldman and Hinshaw,[33] but no experimental evidence was found to substantiate it. Infected animals treated with promin and subsequently reinfected showed no significant modification of their disease as compared with control groups. Promin was found to be tuberculostatic, or suppressive, in its action, not tuberculocidal. Nevertheless, the authors believe that a drug that "serves only a suppressive function does not speak against its practical therapeutic efficacy," and they call attention to the therapeutically valuable but merely suppressive roles of quinine and atabrine in malaria.

Clinical studies with promin-mist inhalations have been continued by Edlin and his co-workers.[34] The technic for the administration of these mists is still being perfected, and only a small number of cases have been investigated. Twenty-four patients were given promin inhalations (a 40 per cent solution at pH 5.6–6.0) in divided doses up to 3.0 gm. daily, for a total average dose of about 200 gm. Cyanosis appeared in 23 of these cases, and anemia in 12. There was some evidence that these inhalations were of benefit in cases of endobronchial ulceration, but its value in the therapy of parenchymal disease was questionable.

The role of diasone as a therapeutic agent is also unsettled. According to the late Dr. Raiziss and his colleagues[35] diasone is less toxic for mice, rats and rabbits than most of the well known sulfonamides and far less toxic than diaminodiphenylsulfone. On the other hand, diasone appears to be appreciably more toxic for human beings. One death attributed to diasone has already been reported,[36] and two other fatalities have occurred during the course of diasone therapy.[37] Skin lesions, especially, must be regarded as potentially serious and warrant immediate discontinuation of the drug.

Therapeutically, the results with diasone are far from dramatic. At the State of Vermont Sanatorium for Tuberculosis, sputum conversion from positive to negative was obtained in only 4 of 21 patients treated with the drug.[37] Pfuetze and Pyle[38] also admit "some disappointment" with diasone treatments. The sharpest indictment of diasone as a therapeutic agent, however, comes from Corper and Cohn.[39] Their experimental evidence leads them to believe that diasone causes an anoxia of the arterial blood and of the internal organs of susceptible animals and that the antituberculosis action of the drug is directly related to this cyanosis and tissue anoxia. The authors therefore conclude, "It would not seem warranted to continue human experimentation with these drugs at present because of the hazards of their use in the tuberculous and the fact that all the necessary information can be obtained from careful animal experimentation."

Because the sulfones have proved themselves either too toxic or too indecisive in their action, attention is turning from them toward the antibiotics. Penicillin, the most important member of this class of substances, is without effect in tuberculosis, but it may be an aid in the treatment of mixed (tuberculous and pyogenic) empyemas. Hirshfeld and his co-workers[40] cite the case of a patient with bilateral pulmonary tuberculosis in whom a pyogenic empyema developed following an intrapleural pneumonolysis. Penicillin, ad-

ministered intravenously and intrapleurally, kept the empyema in check, permitted the completion of a thoracoplasty and enabled the patient to be discharged to her home. A similar experience with penicillin in mixed empyemas following pneumothorax is reported by Howlett and Lester.[41] Penicillin, prophylactically, can also be used with reasonable success in the preoperative and postoperative periods in cases of lobectomy and pneumonectomy as a means of preventing empyema.[42]

So new is the discovery of tuberculocidal antibiotics that research on practically all of them is still in the experimental stage. The one noteworthy exception is streptomycin, isolated from *Actinomyces griseus* by Waksman and his group[43–45] at the New Jersey Agricultural Station. Streptomycin is similar to another related antibiotic, streptothricin, in its bactericidal activity against gram-negative bacteria, its low toxicity and in its in-vitro inhibition of tubercle bacilli.[45, 46] Streptomycin is the first of the newer antibiotics whose toxicity is so low and its in-vitro tuberculocidal activity so definite as to warrant testing in guinea pigs. In these animals its action is comparable to that observed with the sulfones, — its tuberculosis-suppressive effect is "striking," — and most encouragingly, it appears to be well tolerated.[47] Reports on the effect of streptomycin on human tuberculosis have not yet appeared, but clinical trials on 22 patients have been under way since December, 1944.[48]

Other antibiotics that are believed to possess antituberculosis activity are being discovered at so rapid a rate that it is only possible to make brief mention of them. Asheshov and Strelitz[49] have obtained a tuberculocidal product from the fungus *Aspergillus fumigatus*, and in-vitro tests show that even impure preparations are active in dilutions up to 1:500,000.[50] Gerber and Gross[51] and Kurung[52] have also reported inhibition of the growth of tubercle bacilli by presumably other products from molds belonging to the family Aspergillaceae. Other investigators[53] have found that buttercup juice stops the in-vitro growth of human tubercle bacilli, but the toxicity of the juice for laboratory animals is so great that therapeutic tests have been impossible.

Miscellaneous Topics

Bacteriology. When tubercle bacilli are inoculated into the chorioallantoic membrane of a chick embryo, they grow rapidly and the character of the lesion that results varies somewhat with the type and virulence of the injected bacillus. It had been hoped that chorioallantoic-membrane cultures could be used for testing grades of virulence. Fite and Olson[54] inoculated forty-six different strains of acid-fast bacilli into chick embryos and concluded from these tests that organisms of high virulence grew most rapidly and that avian and bovine tubercle bacilli produced characteristic lesions. Unfortunately, however, the chorioallantoic membrane varies too widely in response to avirulent acid-fast bacilli to make the procedure, by itself, of value in determining the virulence of a given strain or its species.

Emmart and Seibert[55] have taken advantage of the chick embryo to test the tuberculostatic action of various serum fractions obtained from normal, "sensitized" and tuberculous rabbits. Serum from tuberculous rabbits and from those sensitized with a purified tuberculoprotein preparation possessed tuberculostatic activity, as determined by the size and development of tubercles on the chick embryo. Pooled serums of patients with minimal tuberculosis contained a gamma globulin that also seemed to possess a tuberculostatic effect, although the data, according to these investigators, "were insufficient to be statistically significant."

The problem of the morphology of tubercle bacilli, especially the question whether they exist in forms other than acid-fast rods, is still unsettled, but the work of Alexander-Jackson[56] during the past ten years has brought forth considerable evidence to support the hypothesis that globoid and coccoid nonacid-fast forms do exist. These are described as a "zoogloeal plasmodium consisting of granules or larger globoid bodies surrounded or enmeshed by amorphous material." These zoogloeal forms can be seen in unstained material or by special staining technics.[57] Photographs taken with the electron microscope indicate that they are able to revert to rod forms, and vice versa. Minute, virus-like tubercle bacilli, on the other hand, probably do not exist. According to the researches of Soltys and Taylor,[58] tubercle bacilli are retained by Gradocol membranes of known pore diameter that allow ready passage of the ultravisible viruses.

Within the past few years the technic of fluorescence microscopy has improved to such an extent that the method can now be regarded as being available for routine laboratory use in the detection of tubercle bacilli in sputum or other excretions. Lempert,[59] in an excellent review, discusses the principles underlying fluorescence microscopy, as well as the practical, laboratory setup. In comparing this method with the Ziehl–Neelsen staining technic on three hundred specimens, Lempert finds the former is faster and at least equally as accurate as the latter. In addition it is neither expensive nor difficult. Voigt[60] prefers the luminescence technic, since a greater number of organisms can be detected in sputums by this method than by the usual staining methods. In tissue sections, too, Tanner[61] finds more organisms by fluorescent staining than by using the regular fuchsin stain. Curiously, neither method appears capable of staining all the organisms in a given field. Tanner believes that there may be additional organisms that are never stained by any of the present methods.

Air-borne tuberculosis. The respiratory route is regarded as the path usually taken by tubercle bacilli in their invasion of the human body. Therefore, the respiratory route might be used as a path for experimentally infecting tuberculosis-resistant animals. Glover[62] has demonstrated that mice, regarded as resistant, can be infected with tubercle bacilli if the germs are dispersed in fine vapors or aerosols. Quantitative tests have shown that, by the respiratory route, one hundred inspired bacilli will infect some mice; one thousand bacilli will infect practically all.

Since tubercle bacilli are so often air-borne, it would seem that, if sterilization or disinfection of the air could be effected, the incidence of the disease might be reduced. Lurie[63] has shown that rabbits can, to a great extent, be protected against natural air-borne, contagious tuberculosis by ultraviolet sterilization of the air. Potter[64] has conducted several experiments that indicate that the glycol aerosols — chemical agents that have been proved bactericidal against numerous other air-borne bacteria — can also kill tubercle bacilli. Coating the bacilli with a thin film of mucus, as under natural conditions, apparently does not prevent their extermination by glycol aerosols. He concludes: "We have in the glycols, agents which are broader in their action than the sulfonamides. Although purely preventive and not curative in action, I feel that, in the long run, the glycols may well strike us as having human importance equal to that of the sulfonamides or even greater."

Carbon dioxide for cough. For the past few years, Banyai and his associates[65, 66] have urged that carbon dioxide inhalations be employed as a therapeutic measure for cough and dyspnea that would otherwise be uncontrollable. A mixture of carbon dioxide (10 per cent) and oxygen (90 per cent), it is claimed, liquefies the mucopurulent exudate in the bronchi, reduces its viscosity and converts a harsh, nonproductive cough into a loose, productive one. Treatments vary in length from five to fifteen minutes, and the inhalations are administered once, twice or three times a day. In the beginning, treatments are given daily; later, the frequency of the inhalations can be reduced. The liquefying effect of carbon dioxide is said to be greater than that of the more frequently used expectorants. Treatment with carbon dioxide inhalations apparently deserves a wider application than it has as yet received.

Rehabilitation. The rehabilitation of persons with tuberculosis is a serious problem. Since tuberculosis is a chronic disease, exact information regarding survival rates should be obtained before determining the type of rehabilitation best suited to the individual patient. Factors such as age, sex and occupation must be included in evaluating the prospects for suitable rehabilitation. Hilleboe[67] has reported on the survival rates for approximately 10,000 patients in the third decade as correlated with the stage of the disease and the presence or absence of tubercle bacilli in the sputum. A negative sputum at the time of discharge from the sanatorium seemed to be the most important single factor favorably influencing the survival rates. Even those patients whose disease was far advanced but whose sputum was negative had the relatively high survival rate of 79.1 per cent at the end of the six-year period of study. He states, "Rehabilitation can become an important factor in further reduction of the mortality rate from tuberculosis in the United States."

Fever therapy in paresis and tuberculosis. Hyperpyrexial (malarial) therapy for paresis has been traditionally regarded as contraindicated when the paretic also has pulmonary tuberculosis. Pleasure[68] finds no real evidence to support this viewpoint, neither from a survey of the literature nor from his own experience. In his series of 11 cases, only 1 patient showed a spread of the tuberculosis following fever treatment. He therefore concludes that malarial therapy per se is not contraindicated in active pulmonary tuberculosis and that patients with both syphilis of the central nervous system and tuberculosis of the lungs should not be denied the benefits of hyperpyrexial treatment.

Childhood tuberculosis and unrestricted activity. Levine[69] has studied 90 children with primary tuberculosis, 27 of whom went through the active phase of the primary complex before they were twelve months of age and were therefore regarded as nonambulatory. Sixteen of these children died. Of 60 older and ambulatory infants only 4 died of tuberculosis. There were 3 additional patients in this older age group who were hospitalized. Study of these groups of children indicated that activity does not lengthen the course of the disease or increase the complications. He states, "An analysis of the histories of the children in this series demonstrates that the age of the children at the time of infection, rather than the method of treatment, is the important factor in mortality from primary tuberculosis in early childhood." Rest in bed should be limited only to periods when the temperature is elevated, as would be advised in any febrile condition.

Spontaneously healing cavities. Dunner[70] has described the roentgenologic appearance of a type of tuberculous cavity that tends to heal spontaneously. It is thin-walled, occurs in various regions of the lung and is generally situated in a field of small nodules of the miliary type and of even distribution. Sixteen cases are reported. Clinical signs of cavity or spread are usually absent. If Dunner's observations can be confirmed, these criteria will provide valuable aids for forming a reliable opinion concerning the prognosis and for furnishing a certain guide to therapy in many of these difficult advanced cases of cavitation.

Vaccines and serums. In spite of some recent evidence favoring their use, the status of vaccines for the prevention of tuberculosis is still questionable. A report from Brazil on the work with BCG immunization in children from 1927 to 1944 includes some data on 161,152 immunized children and an additional 3000 anallergic persons in other age groups.[71] Although the technic of immunization and the immediate response to inoculation are described, no conclusions are given concerning the prophylactic value of the method.

The data from Chicago are more specific on this point. There, under the direction of the staff of of the Municipal Sanitarium, a ten-year study of BCG prophylaxis involving 2515 children has been conducted.[72] In 1204 vaccinated children in whom no source of contact with tuberculosis was known, there were 3 cases of tuberculosis and 1 death from the disease. On the other hand, in 1213 unvaccinated controls, there were 23 cases of tuberculosis and 4 deaths. Similarly, in 98 vaccinated newborn infants with known contact to tuberculosis, only 1 developed the disease and there were no deaths; whereas in the unvaccinated group of 63 cases, 4 children developed tuberculosis and 3 died. Considering the groups as a whole, there were 27 cases of tuberculosis and 7 deaths in the unvaccinated group as compared with 4 cases and 1 death in the vaccinated. These studies indicate that BCG may have a definite prophylactic value, especially in the early years of life.

Vaccination may also prove worthwhile in special groups of the adult population, such as inmates of hospitals for the insane. At the Mental Hospital in Kingston, Jamaica, for example, tuberculosis causes 25 per cent of all deaths and 86 per cent of those with clinical tuberculosis develop the disease while in the institution. In this tuberculosis-ridden population, Wells and his co-workers[73] have been experimenting for more than ten years with a heat-killed vaccine. They found that both the attack and death rates for tuberculosis were significantly lower among recipients of the vaccine administered intracutaneously than among persons alternately chosen but not vaccinated, who served as controls. It was observed, too, that those persons who had a positive tuberculin test on admission also had lower attack and death rates than those with weak or negative reactions, vaccinated persons and the controls. The suggestion is advanced that vaccination may be of value in other groups that are exposed to an unusual risk of tuberculous infection, such as medical students, nurses, attendants and contacts.

In a recent paper, Chadwick[74] makes mention of the investigations of Dr. Cleaveland Floyd on "fractions of the tubercle bacillus that have not been used before in treatment." The fraction that is currently being studied is said to prevent the development of the disease when injected into previously infected animals. Early results on a few patients are regarded as encouraging, but no definite report has as yet been made. The Boston Tuberculosis Association has taken an active interest in this work and is making efforts to obtain the financial support that the project deserves.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 31421

PRESENTATION OF CASE

A thirty-seven-year-old woman entered the hospital complaining of diarrhea.

Eleven years previous to admission she had her first attack of diarrhea, with several liquid stools daily, without blood, pus or mucus. She was nauseated and had periumbilical cramps, which were relieved by evacuation. The first episode lasted about six weeks. A year later, and again four years later, she suffered similar attacks of diarrhea. Following her third acute episode, she had about three semiformed stools daily, without abdominal cramps or weight loss. Nine weeks before admission, diarrhea recurred, with as many as ten watery stools daily. Nausea and cramps were present. A lemon-sized mass was noted in the right lower quadrant; at times it became enlarged and then decreased in size spontaneously with audible gurgles. Five weeks before admission, because of persistence of the above symptoms, and because a barium enema had shown an obstruction in the region of the cecum, an ileocolostomy was done at another hospital. Two weeks later the mass in the right lower quadrant, which had continued to increase in size after the operation, ruptured through the upper end of the incision and began to discharge small-bowel contents.

The patient was markedly emaciated, pale and dehydrated. Examination of the heart and lungs was negative. The abdomen showed a fistula at the upper end of a lower right rectus incision.

The blood pressure was 110 systolic, 70 diastolic.

Examination of the blood showed 8 gm. of hemoglobin and a white-cell count of 7200, with 70 per cent neutrophils. The red cells showed considerable achromia, with moderate variation in size and shape. The urine was normal. The nonprotein nitrogen was normal. The total serum protein was 4.4 gm. per 100 cc., and the chloride 94 milliequiv. per liter. A barium enema passed only to the hepatic flexure (Fig. 1), beyond which point the patient could not tolerate the enema. No fistula was evident. No true shelf was seen at the end of the barium column. A Miller–Abbott tube was inserted, and on fluoroscopy was found to have descended to the cecum. Barium was then introduced into the bowel through it. The ascending colon was normal, but the barium did not pass the region of the hepatic flexure. The point of entry of the fistula into the bowel was not demonstrated. Although it seemed shrunken, the cecum filled with barium and the ileocecal valve opened. Another barium enema was given. The normal haustra of the colon were not evident, and the colon seemed to be somewhat shortened. There was no definite rigidity of the wall, and no ulcerations or granulations could be seen. Barium did not pass the hepatic flexure. When the colon had emptied, long areas of segmentation were seen (Fig. 2).

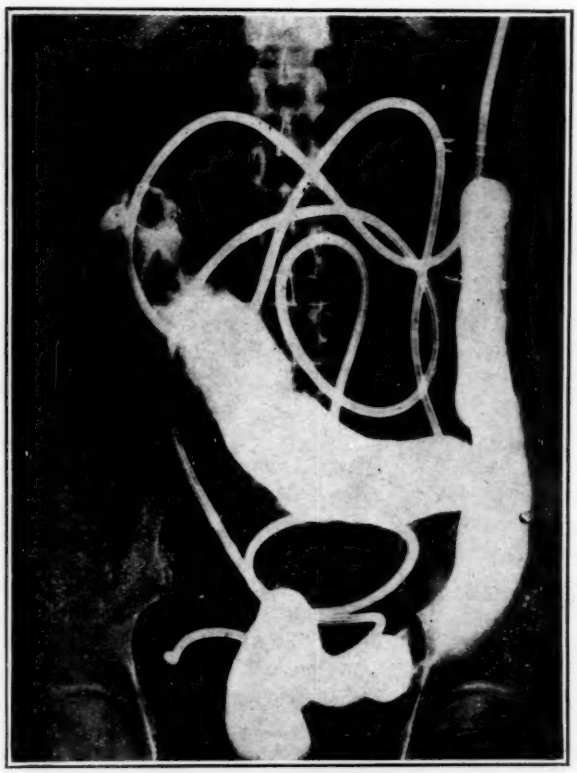

FIGURE 1. *Roentgenogram of Bowel following a Barium Enema.*

Note the abnormal haustra and the obstruction in the region of the hepatic flexure.

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. EARLE M. CHAPMAN: It seems fairly clear that some process was causing obstruction, probably in the region of the hepatic flexure. The lemon-sized mass was the dilated cecum resulting from the low-grade obstruction. When that went down everything subsided, but this had been going on for many years. Finally an ileocolostomy was done at another hospital, which, I assume, was an error

*On leave of absence.

because it joined the bowel to the cecum just below the point of obstruction and nothing was accomplished.

May we see the x-ray films?

DR. MILFORD D. SCHULZ: The chest film shows evidence of an old tuberculous lesion in the right apex. On this film, taken at the time of the first barium enema, one can see that the bowel is short-

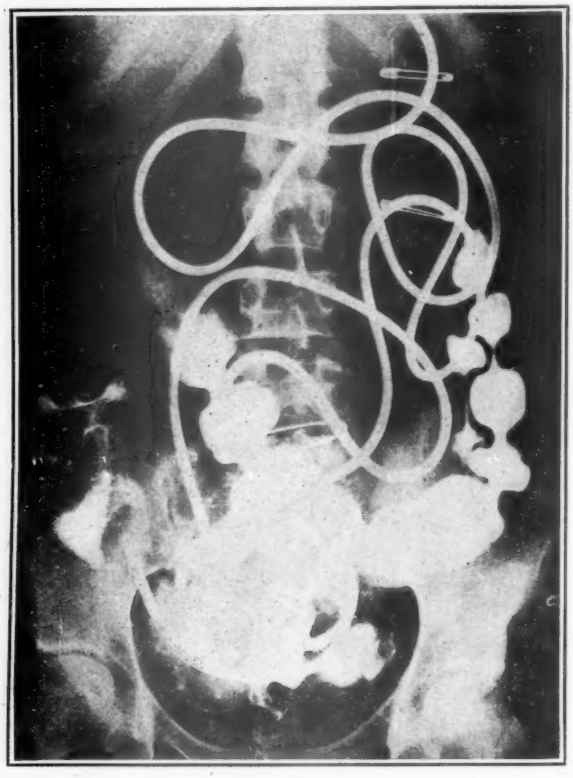

FIGURE 2. *Roentgenogram of Bowel following a Barium Enema.*
Note the segmentation of the bowel.

ened and has no normal haustra. No barium passed beyond the hepatic flexure. On the second examination, similar observations were found and one can see a curious segmented appearance when the bowel had emptied.

DR. CHAPMAN: Do you attribute any particular significance to the segmentation?

DR. SCHULZ: It is an abnormal appearance, somewhat similar to what is seen in an unused bowel, although here one wonders about colitis. There are no definite ulcerations. If it is colitis, it is of long standing with scarring. The cecum does not seem to be definitely abnormal. Barium was introduced through a Miller–Abbott tube, but there is no apparent fistula and the barium does not go beyond this point, which is in the region of the hepatic flexure. The cecum itself does not look definitely abnormal.

DR. CHAPMAN: Is that the normal pattern of contraction of the cecum? The contraction of an empty bowel on a small bolus.

DR. SCHULZ: It may be quite normal. I do not believe that the colon as a whole is normal; I can see no evidence of a fistula in these films nor of a short circuit.

DR. JACOB LERMAN: What was the operation? Did they do a cecostomy or a transverse anastomosis?

DR. CHAPMAN: Presumably it was a junction of the ileum and the cecum, and they closed her up tight. The wound broke open, and Nature took care of things, performing a spontaneous ileostomy, that is, if I interpret these findings properly. Am I correct, Dr. Castleman?

DR. BENJAMIN CASTLEMAN: Yes.

DR. CHAPMAN: Dr. Schulz, you are not going to give us any diagnosis on the basis of your observation?

DR. SCHULZ: One is only justified in saying that the patient had an obstructing lesion in the hepatic flexure, the nature of which is not determined. The colon is abnormal; there was probably a colitis.

DR. CHAPMAN: There is no evidence of an active lesion in the lungs?

DR. SCHULZ: I do not believe that the lesion is active.

DR. CHAPMAN: To come to the point, one has to decide what was the process at the point of obstruction in the large bowel in this woman of thirty-seven. The procedure is to review the causes of chronic intermittent diarrhea and to list them in the order of likelihood.

Now that I have seen the chest film, with the x-ray evidence of tuberculosis at the apex, my first choice is tuberculous infection. The chance that this woman had a tuberculous mesenteric adenitis following the lesion in the chest when she was in her early twenties, which subsequently caused a cicatrizing scar in this region, is good. There is no possible way from the evidence at hand to prove this diagnosis.

Another thing that we must think of is that there were adhesions, not due to infection but to some mechanical process that had gone on previously. There is no history of a previous operation for appendicitis. Was there a scar of an appendectomy in the right lower quadrant?

DR. CASTLEMAN: It is not mentioned in the record.

DR. CHAPMAN: The appendix has not been described in these films.

I am reminded of the history of the case of a fifty-two-year-old man who recently came in because of intestinal obstruction, with a mass in the right lower quadrant. Of course, we thought that it was probably a tumor. When he was explored, the operator found a cicatricial band from an old appendectomy entirely encircling the cecum. He made a complete recovery.

When we think of some of the physiologic causes of chronic intermittent diarrhea in young women, one of these is gastrogenic in origin, resulting from a low hydrochloric acid in the stomach; but that is entirely unlikely with this picture. Endometriosis can do queer things. It is said that 10 to 20 per cent of all women between the ages of thirty and the menopause have some degree of endometriosis; these implants frequently land on the sigmoid, in the rectal region or low in the pelvis. The hepatic flexure is a rather unlikely location for an endometrial implant. This is the first case of a woman that I have discussed at a clinicopathological conference in which the record has failed to mention the catamenia. Were the attacks of obstructing pain coincidental with menstruation?

DR. CASTLEMAN: Apparently not.

DR. CHAPMAN: There are other sorts of physiologic abnormalities that can explain these symptoms, such as pancreatic disease. With some abnormality in pancreatic function she could have had a sprue-like disease, but I hardly see how it could have caused an obstruction at the hepatic flexure.

How about congenital disorders? She was quite well advanced in years to have had a congenital disorder. Of course, a Meckel's diverticulum might have caused it in some way, or a volvulus or some sort of queer bands of adhesions in the intestine. All these seem unlikely. Can Dr. Schulz rule out intussusception in these films?

DR. SCHULZ: There is nothing to indicate intussusception.

DR. CHAPMAN: Then we come to the last one in the series that we have to consider, that is, a new growth of some type. New growths are not so common in this region as in the sigmoid and rectum, nor do I believe that carcinoma of any type could have been present for eleven years. The patient was relatively young, thirty-seven years, and the picture she presented does not favor malignant disease; it is just the picture of a patient with poor nutrition due to chronic, intermittent, large-bowel obstruction.

Now that I have gone through all these possibilities, I am going to return to my first choice. I believe that this woman, who had tuberculosis in the right apex at the age of twenty, probably had a small area of tuberculosis somewhere in the abdomen that had become adherent to the serosal surface. A tuberculous lesion there could gradually contract through the years and finally cause obstruction.

I have not even mentioned ulcerative colitis, because I do not believe that the patient had this disease. The x-ray appearance is not that of ulcerative colitis. Dr. Schulz says it is the appearance of an unused bowel.

DR. SCHULZ: I do not believe that one can rule out ulcerative colitis on this appearance.

DR. JOSEPH C. AUB: How about regional ileitis?

DR. CHAPMAN: I did not mention it because I do not believe that this disease was in the ileum. We must accept the fact that the obstruction was in the cecum.

DR. AUB: I agree.

DR. SCHULZ: It was in the cecum or above the cecum?

DR. CHAPMAN: In the hepatic flexure.

A PHYSICIAN: Was a guaiac test done on the stool?

DR. CASTLEMAN: I think that it was positive.

CLINICAL DIAGNOSES

Chronic ulcerative colitis, with adenocarcinoma of hepatic flexure.

DR. CHAPMAN'S DIAGNOSES

Pulmonary tuberculosis, old.
Tuberculous colitis.
Intestinal obstruction from tuberculous scars and adhesions.

ANATOMICAL DIAGNOSES

Chronic ulcerative colitis.
Adenocarcinoma of hepatic flexure.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Dr. McKittrick operated on this patient and found so many adhesions in the right lower quadrant that he was unable to decide what had been done at the earlier operation. He thought that the entire bowel was abnormally thickened. The serosa over the bowel was thickened, and he believed that this was probably due to ulcerative colitis. In the region of the obstruction, he felt a large mass in the bowel, which appeared to be a carcinoma. He therefore performed a transverse ileocolostomy as the first stage for relieving the obstructing lesion.

The patient went home and came back later, at which time he removed the right colon including the hepatic flexure. The obstruction proved to be a completely annular adenocarcinoma; there were no metastases to the regional nodes, although the surrounding lymphatic vessels over the tumor in the wall of the bowel were involved with tumor. The rest of the bowel that he resected showed chronic ulcerative colitis. There were numerous healed ulcers with pseudopolyps of mucosa, such as one sees in the characteristic form of ulcerative colitis. So this was a case of chronic ulcerative colitis on top of which an adenocarcinoma had developed.

CASE 31422

PRESENTATION OF CASE

First admission. A twenty-three-year-old man entered the hospital complaining of diarrhea.

Eleven years previous to admission he had suffered from an acute attack of colitis caused by a

Flexner dysentery bacillus. He was bedridden for about six months, and at the end of that period his stool cultures became negative. During the next two years he had had bloody, mucoid stools, often as many as twelve daily. The number had slowly decreased, and on entry he was having about four a day. During the three years before admission there had been no blood or mucus in the stools. At one time his weight was 50 pounds, but this had gradually increased to an admission weight of 130. He had frequently had slow-healing ulcers on the legs.

Physical examination revealed a pale, poorly nourished man. The fingers and toes showed slight clubbing. There was slight tenderness in the right upper quadrant of the abdomen on deep inspiration.

The temperature was 98.6°F., the pulse 80, and the respirations 20. The blood pressure was 110 systolic, 70 diastolic.

Examination of the blood revealed a white-cell count of 6600, with 75 per cent neutrophils, and 12 gm. of hemoglobin. The urine was normal. A blood Hinton test was negative. The stool was fluid, light brown, neutral in reaction, negative for mucus and gross blood but strongly guaiac positive; no parasites were found on repeated examinations. A barium enema revealed saw-tooth irregularities of the colon throughout its course, including the cecum. There was marked granularity of the mucosa. No filling defects were seen, and the colon was not tender. The ileocecal valve was narrowed and rigid for a distance of 3 to 4 cm.; proximal to this the terminal ileum did not appear unusual. The liver was enlarged and overlay the right iliac crest. Proctoscopic examination showed an edematous, thickened, red and roughened mucosa. In the lower sigmoid was a red, partly ulcerated area occupying about half the circumference of the bowel and composed of a number of polypoid nodules. The bowel wall at this site was flexible.

The patient was discharged on a high-vitamin, low-residue diet, with supplementary vitamins and iron.

Second admission (one year later). The patient was readmitted for study. He had been leading a regular, quiet life and had been having about five stools daily.

Physical examination revealed marked clubbing of the fingers and toes.

Examination of the blood revealed a hemoglobin of 10.5 gm. The stools gave a ++ guaiac reaction. A barium enema passed slowly but steadily from the rectum to the cecum, instead of in the usual segmental manner. There was some shortening of the colon, with several areas of moderate narrowing. There were multiple ulcerations throughout the entire colon. The ileocecal valve appeared thickened. Definite ulceration was seen in the distal 10 cm. of the ileum. Sigmoidoscopy revealed a narrow lumen and a stiff bowel wall. The mucosa was irregular and granular with fibrotic elevations 1 to 2 mm. in height. One area in the sigmoid was dark brown.

The patient was discharged on 5 gm. of sulfathalidine daily.

Third admission (six months later). The patient's condition had remained essentially unchanged. Sulfathalidine was discontinued one week before admission. The stools had been loose, yellow and often watery. His weight was 138 pounds, which he considered normal.

On admission a stool specimen was liquid and tan and gave a + guaiac reaction. The red-cell count was 3,120,000, and the hemoglobin 5.7 gm.

He was discharged on sulfathalidine.

Final admission (eighteen months later). Four weeks before admission the patient, who was then twenty-six years old, had experienced an increase in the number of stools to 6 daily, with cramps just before evacuation and blood in the stools. He had been working hard and tired easily. He began to lose weight. Two weeks later he noted the onset of severe pain in the right upper quadrant and right flank; it was not colicky and was intermittent. A day or two later a pain like a "muscle stitch" appeared in the left upper quadrant. Both pains disappeared spontaneously ten days before admission, leaving no residue. He had had no fever, nausea or vomiting.

Physical examination showed evidence of recent weight loss and a haggard appearance. The tongue was bright red at the tip and edges, with some loss of papillae. The heart and lungs were normal. A superficial, lobulated, firm, nontender mass was felt in the right upper quadrant. It extended into the right lower quadrant and was palpable in the right costovertebral angle. It was fixed to lateral motion but descended on inspiration. Peristalsis was active. Many external hemorrhoids were found. The right leg and thigh were somewhat greater in circumference than those on the left. The reflexes were physiologic.

The temperature was 98.6°F., the pulse 90, and the respirations 20. The blood pressure was 120 systolic, 80 diastolic.

Examination of the blood revealed a hemoglobin of 11.6 gm. and a white-cell count of 10,300, with 58 per cent neutrophils. A blood Hinton reaction was negative. The urine was normal. Stool specimens were dark brown and guaiac negative. The prothrombin time was 30 seconds (normal, 18 to 20 seconds). The nonprotein nitrogen was 22 mg. per 100 cc., the total protein 6.3 gm., and the chloride 105 milliequiv. per liter.

The abdomen became distended, but peristalsis remained active. There was occasional upper abdominal pain, without cramps. Ascites appeared. There was no icterus. A right femoral phlebothrombosis developed. The patient remained weak and despondent. He became nauseated and vomited

all food. The temperature remained normal. He went into coma and expired on the twentieth hospital day.

Differential Diagnosis

Dr. Joseph Aub: This patient had a prolonged disease. It could have been ulcerative colitis or tuberculosis or possibly amebic infection. The unequivocal statement is made that this man had an infection with the Flexner organism. A Flexner infection would not have lasted so long, but it may well have been an ulcerative colitis following a Flexner infection.

The description of the tongue indicates a vitamin deficiency, which is to be expected in this disease.

"A superficial, lobulated, firm, nontender mass was felt in the right upper quadrant." I take that to be the liver. We know that the liver was enlarged three years previously. Of course, it may have been a neoplasm in the liver, but I assume that the mass represented a large liver.

This man undoubtedly had an ulcerative colitis, which may or may not have started from the Flexner infection thirteen years before. A lot of work has been done on this causal relation, although few cases have been proved to follow this infection, and the organism does not appear to be present in many cases of established colitis. At any rate, this man had had ulcerative colitis since he was twelve years old. We must then go into the refinements of the case, where we are apt to be wrong. Everything that Dr. Chapman said in discussing his case holds for this one, and I am not going to repeat. This is not a case of regional ileitis, because the whole large bowel was involved. The crux of the problem is, What did this patient die of, in addition to the ulcerative colitis, and why did he have a large liver for three years?

Are any x-ray films available?

Dr. Castleman: None were taken on the final admission, and the previous ones are not available.

Dr. Aub: When the cecum and ascending colon are so markedly involved, one always thinks of tuberculosis of the large bowel. This lesion started in a twelve-year-old child and might well have been due to tuberculosis. With chronic ulcerative colitis, many polyps form in the cicatricial tissue, and in these areas neoplasm develops at least four times as frequently as it does normally. Ulcerative colitis is certainly one of the precancerous lesions, and the presence of cancer should always be considered in protracted cases. This young man might have had a cancer, but he had a large liver for three years before he died, and I think that it is highly unlikely that a neoplasm from a polyp, even though it may be dormant for a long time, could have reached the stage of metastasizing to the liver and could have remained there for three years before his death. I am willing to rule that out, saying that, although he may have had a carcinoma, the large liver, which is the crux of this problem, was not due to a neoplasm. The clubbing of the fingers might have been caused by the chronic ulcerative colitis and vitamin deficiency or might have been due to liver damage, although I think that the former is the more probable.

Let us discuss the large liver further. Was this cirrhosis? It might have been a cirrhosis dependent on chronic vitamin B deficiency, the type of cirrhosis that can be produced in the laboratory by an inadequate diet plus a toxin of some sort. It could have been that, but at the end of three years, if it was the usual type of portal cirrhosis, the liver should not have been so large. The diagnosis is a difficult choice between cirrhosis of the liver and amyloid disease associated with chronic infection, such as tuberculosis of the large bowel. Amyloid disease can produce this picture; in fact, the amyloid disease sometimes includes the large bowel. The difficulty is that no albumin was found in the urine, which is against the diagnosis of amyloid disease; but there are cases of amyloid disease that do not involve the kidney, which therefore do not have albumin in the urine.

I think that the liver was seriously damaged but not so severely that there developed a high amino acid concentration in the blood stream. At least the nonprotein nitrogen was normal. That he had something wrong with the blood flow through the liver is suggested by the hemorrhoids, the phlebitis and the ascites.

I am perfectly willing to make a diagnosis of chronic ulcerative colitis. This was probably on the basis of the Flexner infection, but it may well have been of tuberculous origin. The large liver was either cirrhotic or amyloid, and I shall say that it was amyloid, although I am probably wrong because it is relatively rare. The amyloid disease did not involve the kidney, although it may have involved the bowel. I think that he also had thrombophlebitis, which was probably ascending and may well have involved the lower veins in the abdomen. Since he kept on urinating, it is probable that it had not reached the kidney veins. He had ascites and vitamin deficiency.

Dr. Earle M. Chapman: I should like to know why Dr. Aub did not consider pylephlebitis, since the man had chronic infection in the bowel, thrombophlebitis and a "sick" liver. He may have had an infection in the portal system.

Dr. Aub: He may have had.

Dr. Jacob Lerman: The patient had no fever.

Dr. Aub: The terminal ascites is interesting. I did not mention several things. Of course, one can always go far afield and bring in everything just to be sure of mentioning what might turn out to be the right diagnosis. These patients are apt to have local perforation of the intestine. But this one continued to have intestinal peristalsis until he died, so it is unlikely that he had a perforation.

I doubt that the ascites was due to pylephlebitis, but I do not know.

DR. LERMAN: I should like to consider hepatoma on the basis of an old cirrhosis.

CLINICAL DIAGNOSES

Chronic ulcerative colitis.
Carcinoma of colon.

DR. AUB'S DIAGNOSES

Chronic ulcerative colitis.
Tuberculosis of large bowel, with amyloid disease of liver?
Thrombophlebitis.
Vitamin deficiency.
Ascites.

ANATOMICAL DIAGNOSES

Chronic ulcerative colitis and ileitis.
Adenocarcinoma of colon (splenic flexure and ileocecal region), with metastases to regional lymph nodes and liver.
Acute bacterial endocarditis: mitral valve.
Septic infarcts of heart, kidneys and spleen.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy on this man showed an extremely severe chronic ulcerative colitis. There were also numerous ulcerations in the last 30 cm. of ileum. The large bowel was thickened, and many of the ulcers were partially or completely healed. The rugal folds were thick. In the region of the ileocecal valve was an annular lesion about 6 cm. in length and about 1 cm. in thickness, which on section was grayish white. It had extended through the serosa and had become adherent to several enlarged nodes, which were also grayish white and obviously neoplastic. A similar lesion was found in the region of the splenic flexure. This seemed to be more invasive than the one in the region of the cecum. Sections showed the ileocecal lesion microscopically to be a low-grade adenocarcinoma, whereas the one in the splenic flexure was an extremely malignant tumor, showing no acinar arrangement and invasion of the veins throughout that portion of the bowel. The liver was tremendous in size, weighing 4200 gm., and was filled with metastases. There was no cirrhosis.

It is interesting that before this patient died a peritoneoscopy was performed, and we made a diagnosis of hepatoma on a biopsy of one of these nodules. The reason for this erroneous diagnosis, in retrospect, is that the tumor cells were tremendous in size, some of them having four or five nuclei and having a definite eosinophilic cytoplasm, such as one sees in hepatoma. Also, even in this small biopsy specimen, we found invasion of the hepatic veins, which is quite the rule in hepatoma. When we compared sections of the biopsy with those of the tumor in the region of the splenic flexure, it was apparent that the cells were the same.

On the mitral valve were a large number of bacterial thrombi from which emboli had gone to both kidneys, the spleen and also the coronary arteries. There was a large focus of septic infarction in the heart, and many smaller ones in the kidneys and spleen.

So here we have another case of chronic ulcerative colitis in which two carcinomas developed. You probably know that Bargen of the Mayo Clinic has been writing for years about the association of ulcerative colitis and carcinoma. His series is, I believe, the largest. In one reported in 1928, he[1] claimed that 10 per cent of the cases of ulcerative colitis have true adenomatous polyps and that 2 per cent develop carcinoma, the carcinoma apparently developing through the stage of adenomatous polyps; in other words, there is first a pseudopolyp, just a tab of mucosa surrounding an area of ulceration, then the pseudopolyp develops into a true adenomatous polyp, and finally the adenomatous polyp becomes malignant. Bargen[2] has recently reported 30 more cases. It is interesting that the average length of time from the onset of the ulcerative colitis to the appearance of the carcinoma is seventeen years. In the cases that we have discussed here today the time interval in one is eleven and in the other fifteen years. I believe that in the last ten years we have had 3 or 4 other cases of carcinoma developing on ulcerative colitis. As Dr. Aub stated, this certainly is a definite hazard in a patient with long-standing ulcerative colitis, especially if he has exacerbations of the colitis, since healing and regeneration of the epithelium may lead to the development of a carcinoma.

DR. AUB: You have not explained the big liver that had been noted three years previously.

DR. CASTLEMAN: Most of our cases with ulcerative colitis that come to autopsy have tremendous fatty livers.

The x-ray appearance two or three years before entry was probably due to a low-grade adenocarcinoma in the ileocecal valve. He may have had that for a couple of years, but certainly the one in the region of the splenic flexure was a recent development. It is one of the most rapidly growing carcinomas of the bowel that I have ever seen.

DR. LERMAN: You are definite that it was not a hepatoma?

DR. CASTLEMAN: Yes.

DR. AUB: There was no cirrhosis and no evidence of amyloid disease?

DR. CASTLEMAN: No.

DR. CHAPMAN: I think it is instructive that Dr. Aub and I both missed the diagnosis. I am sorry that Dr. McKittrick is not here, because I should like to know the clinical implications that he would

stress at this point in regard to the way we should take care of these patients with chronic ulcerative colitis. Too often they have an ileostomy and are allowed to go on with the ileostomy; because they are much better, we allow the bowel to lie dormant, which is perhaps not the right thing to do. Perhaps a colectomy should be performed, as Dr. McKittrick has done so often. The colon in ulcerative colitis is frequently the site of cancer. That is the one clinical lesson we ought to carry away with us.

DR. CASTLEMAN: I believe that the practice in the hospital now is that if, after ileostomy, a patient continues to have attacks, colectomy is indicated then and not fifteen or seventeen years later, when it may be too late.

ADDENDUM

DR. LELAND S. MCKITTRICK: The problem of carcinoma of the bowel arising in cases of long-standing chronic ulcerative colitis is an important and disturbing one. My own experience with cancer in these patients is not a large one. I have probably seen 5 or 6 such cases, but in only 1 of these was the carcinoma operable. I do not know the operability in the group that Bargen has described but I suspect that it was low. This is particularly true after an ileostomy has been performed, because the symptoms of obstruction, which are frequently so important in the diagnosis of cancer of the large bowel, are absent and because the bleeding that these patients often have may be misinterpreted as being due to the colitis. Dr. Chester M. Jones and I have frequently discussed the possibility of annual or semiannual examination of the bowel by a barium enema, but this is not wholly practical, one reason being that not infrequently after ileostomy the bowel does not quite empty itself and the barium remains inspissated for indefinite periods.

I feel strongly that the indications for colectomy should be broadened. The mortality following colectomy done as an elective procedure is low. Certainly the demonstration of persistent polyps or pseudopolyps is, I believe, a definite indication for colectomy. At the present time it is my opinion that any large bowel which, after ileostomy, shows persistent evidence of activity of the disease should probably be removed. In many of these cases, the rectum and lower sigmoid are left in place, thus allowing an opportunity for reëstablishment of continuity at a later time, should some method of curing the disease be developed.

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2. Bargen, J. A. Chronic ulcerative colitis associated with malignant disease. *Arch. Surg.* **17**:561-576, 1928.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

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Subscription Terms: $6.00 per year in advance, postage paid, for the United States (medical students, $3.50 per year); Canada, $7.04 per year (Boston funds); $8.52 per year for all foreign countries belonging to the Postal Union.

Material should be received not later than noon on Thursday, two weeks before date of publication.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

REFRESHER COURSES

Although the three medical schools and most of the teaching hospitals in Greater Boston, as well as other hospitals in Massachusetts, have signified their willingness to participate in a program designed to provide refresher courses for discharged medical officers and stale civilian physicians, the consummation of the scheme within a period short of many months appears to be impossible. The obstacle is a lack of teaching personnel, and until such a time as the Army and Navy release an appreciable number of medical officers capable of effective teaching, this well conceived and extremely necessary program must be postponed.

With the end of combat, the need for medical officers must have dropped appreciably, and there seems to be no valid reason for not revising the tables of organization of both the Army and Navy so that they are on a peacetime basis. It is obvious that a certain number of medical officers are needed for the care of the armed forces in occupied areas and of those at permanent Army installations and on the ships of the Navy. On the other hand, these men represent only a small percentage of those who have been serving with the Army and Navy. It will undoubtedly take time to return many of these men to the United States, and more time will be consumed by the formalities of release or discharge; but the sooner this is accomplished the sooner medicine, including postgraduate instruction, will return to a reasonably normal basis.

For the time being, refresher courses must, as a rule, be limited to short periods of intensive teaching, such as the courses to be given this fall in various communities in the Worcester and Springfield areas by teams of instructors under the sponsorship of the Subcommittee on Medical Education, Committee on Postwar Planning. Other examples are the three-day course given periodically at the New England Deaconess Hospital, which covers all the various aspects of diabetes mellitus, and the course in medicine for general practitioners that is to be given by members of the Lahey Clinic in November. This type of instruction is not suitable for the physician who desires extensive postgraduate instruction or training in some particular aspect of medicine, but at the moment, it is about all that can be expected.

ENGLAND WANTS MORE AND BETTER MILK

The Mother of Parliaments, according to a leading article in the April 21 issue of the *Lancet*, is taking seriously the dairy situation in England—the shortage of milk, the shortage of cows, the shortage of veterinarians and the high incidence of diseased cattle. At present the daily per capita milk consumption in Great Britain is 0.58 pint. Before the war it was 0.45 pint, and a suggested target at which to aim has been set at 0.75 pint or, ideally, a full pint.

The discussion, which took place on April 11, was initiated by Viscount Bledisloe in the House of Lords with the statement, "In the matter of the general milk-supply, its quality, the individual milk consumption, the milk yield per cow, bovine disease, veterinary treatment and the number and qualifications of our veterinarians, Great Britain compares unfavourably with most of the other civilised countries of the world, including indeed some uncivilised countries, such as Germany."

One of the alarming statements was that, although various efforts had increased the milk supply by 12 per cent from 1939 to 1945, the prevalence of mastitis, contagious abortion, sterility and Johne's disease had reduced annual production by about 200,000,000 gallons, in addition to the loss of cattle through foot-and-mouth disease. Among the recommendations proposed were the offering of a bonus to increase the number of tuberculin-tested herds, a survey of the incidence of cattle disease and an increase in the numbers of tuberculin-tested herds to the point where eventually milk from a herd that is not free from tuberculosis would not be accepted for human consumption. A further recommendation was that veterinary study be given full university status and that veterinary research should be established in all training centers.

Particularly startling to Americans are the statement that 40 per cent of the cattle of the United Kingdom are infected with tuberculosis and the apparent distrust in which pasteurization is still held. Thus, it is stated in the section "Parliament" of the same issue of the *Lancet*: "Lord Moran applauded Lord Bledisloe's exquisite tact in not mentioning pasteurization. It had always seemed to him that if milk contained organisms . . . and if those organisms produced disease, then the public, when it understood the position, would demand that those organisms be removed. . . . Our target must therefore be to sell milk free from disease or to pasteurize it. If it was sold and bottled on the farm where there was no disease, then pasteurization would die a natural death."

In this country the eradication of bovine tuberculosis has gone steadily forward to the point where now in Massachusetts, with all cattle tested, the rate of incidence is only 0.2 per cent, the rate being 0.5 per cent or less for the country as a whole.* In addition, pasteurization, far from being allowed to die a natural death, has steadily increased until it is practically a *sine qua non* of clean milk. In fact, on September 30, 1943, the health commissioner of Boston took the final step in requiring all milk sold in this city, even from certified herds, to be pasteurized.

*Tuberculosis Eradication Division, United States Department of Agriculture. Personal communication.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

CANNON — Walter Bradford Cannon, M.D., of Cambridge, died at Franklin, New Hampshire, on October 1. He was in his seventy-fourth year.

Dr. Cannon received his degree from Harvard Medical School in 1900, and had served there as George Higginson Professor of Physiology from 1906 to 1942. During World War I he was chairman of the Committee on Physiology of the National Research Council, and went abroad in May, 1917, with the Harvard Hospital Unit. He served overseas until January, 1919, and was discharged with the rank of lieutenant-colonel. In June, 1919, the British government conferred on him the Cross of the Companion of the Bath "for meritorious service for the Allied cause." He was also awarded a citation by General Pershing for instruction in shock treatment in the AEF. He was a trustee and member of the Executive Committee of the Harvard Medical School of China and in 1942 was elected chairman of the Massachusetts Branch of the American Bureau of Medical Aid to China.

Dr. Cannon was a member of the American Medical Association, the American Association for the Advancement of Science, the American Physiological Society, the Society for Experimental Biology and Medicine, the American Gastroenterological Association, the American Philosophical Society of Philadelphia, the American Psychological Association and the Boston Society of Medical Sciences.

His widow, four daughters and a son survive.

HEARN — Walter L. Hearn, M.D., of Lynn, died September 30. He was in his sixty-eighth year.

Dr. Hearn received his degree from Harvard Medical School in 1902. During his career he served on the staffs of the Boston Lying-in Hospital, the Children's Hospital, the Massachusetts General Hospital and Lynn Hospital. He was chief surgeon of the Lynn Cancer Clinic, and in recent years had been Lynn school physician.

MEDICOLEGAL ABSTRACT

Right to Compensation: Right of a physician consulted at the request of a company to charge the patient. The physician sued the patient and her husband for the reasonable value of his professional services, and the defendants prevailed even though they admitted that the services were performed and that the amount claimed was their reasonable value.

The patient sustained a fall in a retail store, and the store manager directed her to see the plaintiff and have him perform such professional services as were necessary due to the fall or accident. The

patient and her husband consulted the physician only after the store manager advised her that she would be put to no expense but that such professional treatment would be "all gratis," and they consulted him only because they had been so directed by the manager. There was evidence that the physician knew of the arrangement before he treated the patient.

It was clear that neither the patient nor her husband had agreed expressly to pay the physician, but the court thought he could recover the reasonable value of his services from the patient if there was any implied contract to pay for them, and under the statute in force there would be such a contract if its existence and terms were "manifested by conduct." The court held that no such contract was implied when the physician assented to the arrangement that had been made with the store. The court said:

> When plaintiff proceeded to treat Mrs. Iverson knowing of the agreement between her and Woolworth's and at Woolworth's request, such conduct rather than implying an understanding between physician and patient that the patient will pay the reasonable value of the services performed, implies, in our opinion, an agreement by the physician to perform the services according to the conditions and terms under which he is consulted and asked to perform the service.

The court made it clear that it was not holding that the physician was necessarily precluded from charging the patient for his services if he had rendered the services at the request of the store. The point was only that the physician could not charge the patient if he had performed the services under an arrangement that the patient should not have to pay for them. — (*Opheim* v. *Iverson*, So. Dakota, 16 N.W. [2d] 440 [1944].)

MISCELLANY

NOTE

The following physicians successfully passed the written examination for fellowship in the American College of Chest Physicians, which was held in June, 1945, and will be awarded their fellowship certificates at the next convocation of the college: Ralph H. Adams, M.D., Boston; Henry A. Hudson, M.D., Marblehead; and David S. Sherman, M.D., Brookline.

MAJOR MARKS AWARDED LEGION OF MERIT

Major George A. Marks, M.C., A.U.S., on leave of absence as a member of the Surgical Staff of the Massachusetts General Hospital, was recently awarded the Legion of Merit. The accompanying citation reads as follows:

> For exceptionally meritorious conduct in the performance of outstanding service in the Southwest Pacific Area from July 11, 1942, to June 13, 1944. Major Marks organized, trained and commanded a portable surgical hospital which was attached to an infantry regiment during the Papuan campaign. Under his exceptional leadership the unit moved in close proximity to front-line troops and achieved a remarkable record in the care of the sick and wounded. It was essentially as a result of his professional ability and guidance that many lives were saved under the most difficult conditions of jungle warfare. Later, as a surgical consultant, he visited hospitals in advanced areas as an instructor and adviser. His knowledge and advice proved invaluable both in the treatment of casualties and in assisting and planning of additional facilities. By his outstanding ability in the field of surgery, Major Marks made a signal contribution to medical treatment in the Southwest Pacific Area.

NOTICES

ANNOUNCEMENTS

Dr. Fred C. Gunter announces the opening of his office at 375 Commonwealth Avenue, Boston.

Dr. Alfred Hurwitz, who has been honorably discharged from the armed services, has resumed the practice of general surgery at 171 Bay State Road, Boston.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, OCTOBER 25

THURSDAY, OCTOBER 25.
Massachusetts Public Health Association. Beth Israel Hospital.

FRIDAY, OCTOBER 26
*9:00–10.00 a.m. Refractory Macrocytic Anemias. Dr. William B. Castle. Joseph H. Pratt Diagnostic Hospital.
*9:00–10.00 a.m. Medical clinic. Isolation Amphitheater, Children's Hospital.
10:50 a.m. Problems of Syphilis in Thoracic Surgery. Dr. John W. Strieder. (Postgraduate clinic in dermatology and syphilology.) Amphitheater, Dowling Building. Boston City Hospital.

SATURDAY, OCTOBER 27
*10.00 a.m.–12:00 m. Medical staff rounds. Peter Bent Brigham Hospital.

MONDAY, OCTOBER 29
*12:00 m.–1:00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, OCTOBER 30
*9:00–10:00 a.m. Medical clinic. Infants' Hospital.
*12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

WEDNESDAY, OCTOBER 31
*9:00–10.00 a.m. The Base Line of Positivity in Skin Tests. Dr. Ralph E. Wheeler. Joseph H. Pratt Diagnostic Hospital.
*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

OCTOBER 1–DECEMBER 10, 1945 and JANUARY 7–APRIL 22, 1946. Metropolitan State Hospital. Eleventh postgraduate seminar in neurology and psychiatry. Page 314, issue of September 6.

OCTOBER 24. New England Society of Physical Medicine. 8:00 p.m. New England Sanitarium and Hospital, Melrose.

NOVEMBER 8. Pitfalls and Pleasures in the Treatment of Diabetes. Dr. Elliott P. Joslin. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

DISTRICT MEDICAL SOCIETY

WORCESTER

NOVEMBER 14. Grafton State Hospital.
DECEMBER 12. Worcester City Hospital.
JANUARY 9. St. Vincent Hospital.
FEBRUARY 13. Worcester State Hospital.
MARCH 13. Worcester Memorial Hospital.
APRIL 10. Hahnemann Hospital.
MAY 8. Annual meeting.